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Postgraduate Medicine

Official Journal of the Interstate Postgraduate Medical Association

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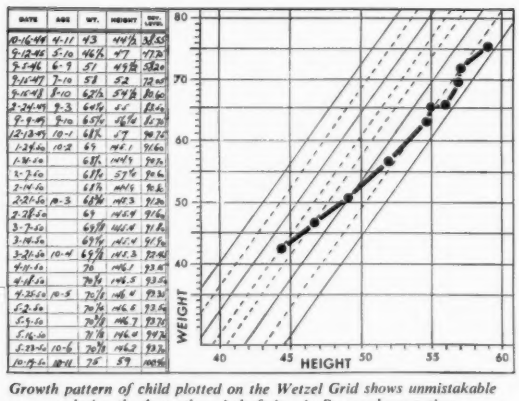

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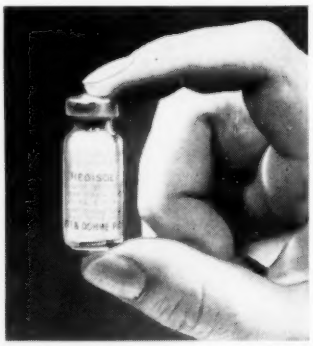

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1. Wetzel, N.C., Hopwood, H.H., Kuechle, M.E. and Grueninger, R.M.: J. Clin. Nutrition, *1*:17, Sept.-Oct., 1952.

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TABLE *of* CONTENTS

SPECIAL ARTICLES

Emotional Factors Involved in the Evaluation of Coronary Artery Disease
DOUGLAS D. BOND, M.D. 487

Vagotomy in the Treatment of Peptic Ulcer
PAUL BANZET, M.D. 491

Surgical Treatment of Osteoarthritis of the Hip
EDWARD L. COMPERE, M.D. 495

Lesions of the Adrenal Glands of Surgical Significance
JAMES T. PRIESTLEY, M.D. AND ROBERT M. SALASSA, M.D. 500

A Simple Method for Detecting the Salt Depletion Syndrome During Cardiac Therapy
JACOB J. SILVERMAN, M.D. 547

The Antiquity of Disease
FREDERICK STENN, M.D. 579

DIAGNOSTIC CLINICS

Splenectomy for Blood Dyscrasias
WILLIAM D. HOLDEN, M.D. 507

A Breast Clinic
ROBERT M. JANES, M.D. 513

Treatment of Pulmonary Tuberculosis
WINTHROP N. DAVEY, M.D. 519

Radioactive Iodine in the Medical and Surgical Management of Goiter
MORRIS T. FRIEDELL, M.D. 523

The Present Status of the Treatment of Gastric Malignancy
SAMUEL F. MARSHALL, M.D. 529

SCIENTIFIC EXHIBIT

The Treatment of Burns by the Exposure Method
CURTIS P. ARTZ, M.D., ERIC REISS, M.D., JOHN H. DAVIS, M.D. AND WILLIAM H. AMSPACHER, M.D. 535

(Continued on page A-6)

PEDIATRICS IN GENERAL PRACTICE

The Newer Drugs and Their Indications in Childhood
E. PERRY CRUMP, M.D. 552

GENERAL PRACTICE REVIEW

The Hard of Hearing Patient
HOWARD P. HOUSE, M.D. 563

Aplastic Anemia
TRUMAN G. SCHNABEL, M.D. 568

DEPARTMENTS

EDITORIALS 574

Aviation Medicine
Household Detergents
Atomic Medicine
The Exact Use of Medical Terms
Asthma in Childhood

INDEX TO VOLUME 13 583

CLINICAL NOTES

7. *Hydrocortisone Acetate* 528
8. *The Core of the Cancer Problem* 534
9. *Causes of Sodium Depletion* 551
10. *Disguising Nauseous Drugs* 562

NEW DRUGS AND INSTRUMENTS 588

LETTERS FROM ABROAD A-12

YOUR QUESTIONS ANSWERED A-20

Pregnancy and Thyroid Cancer
Streptomycin for Infants
Use of Digitalis
Disturbances of Sexual Function
Penicillin

MEDICAL MISCELLANY A-36
Three Dimensional Movies. F. Donald Napolitani, M.D.

THE MEDICAL MUSE. Richard Armour A-38

THE MEDICAL BOOKMAN A-54

DR. PEPYS' PAGES. Morris Fishbein, M.D. A-76

INDEX TO TECHNICAL EXHIBITS A-116

Emotional Factors Involved in the Evaluation of Coronary Artery Disease

DOUGLAS D. BOND*

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Attention is drawn to some of the factors involved in the precipitation of symptoms in coronary artery disease, and some practical illustrations are given as to how emotional understanding helps in the practical management of those symptoms.

SEVERAL facets of the problem of emotional factors in coronary disease are particularly practical and useful. To begin with, it is extremely important to take into account the kind of person who develops a coronary occlusion. I know in a sense this is "old hat," and yet just the other day in the medical wards of our hospital I saw a man who was addicted to alcohol and to cigarets. He had experienced his second coronary occlusion. He had been told after his first occlusion that he would have to take it easy. It had been explained to him that he couldn't even go to a ball game—that he could do practically nothing. (At least his interpretation was that he could do nothing.) He said very frankly, "If you are going to take life away from me, why don't you let me die happy?" It was a hard question to answer.

He was immediately placed on a salt-free diet. Cigarets and alcohol were forbidden, and he was told to sit, rest, be happy, relax and get well. I saw him in preparation for this address, and I would like to communicate to you the feelings this man had. He was, as they say, ready to explode. He was very restless and was ready to leave the hospital immediately.

It was interesting to observe the initial reaction of the medical students who talked with him. They were very much taken aback when he asked them why they didn't let him die happy rather than torture him to death. They also thought there must be some remarkably good reason why the interns had put him on a salt-free diet. I told the students that they would be interns next year and that probably there wasn't too much medical knowledge hidden from them. So many times you rush into the hospital and ask, "What has come in?" You are told, "A coronary." You sit down, and you write out the order: complete blood count, urinalysis, salt-free diet, and so on and so on. This is not done with malignant intent; it is just that it often has a malignant result.

It was apparent that this man's life could be saved, one might say, in a most undramatic fashion. If we had not intervened in the way we did, something unfortunate might have resulted. I said to an intern, "Get a pack of cigarets. Go in and give it to this man. Get a pint of whiskey and go in and sit down with him. Be sure that *he* drinks the whiskey, not you! Talk to him and see if you can get him to stay in the hospital. Because one thing you can be absolutely sure of: If you don't do this, he is going to leave the hospital and get not

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Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

a pint but a quart, and a pack of cigarets or a cigar. And you might just as well face the inevitable in such a case, for you can't change the patient."

You might as well fit your ideal scheme of things to meet the patient's needs. Be practical, in other words—extremely practical. Furthermore, I think many of you know that it is not easy for some persons to sit in bed and relax just because they are ordered to do so. They stew and fret, and probably do much damage to their internal organs if they are thus frustrated.

Another side of the picture is that emotional factors often seem to precipitate a coronary attack. Dr. Joseph T. Wearn, with whom I have talked at great length on this topic, has had a long experience with coronary disease. He reported 23 cases from the Peter Bent Brigham Hospital in 1923, when it was quite unusual to report a series of coronary occlusions with their autopsy findings. The first case was that of a man who was recovering from a coronary infarct and who rose in wrath when a patient across the ward said something unpleasant to him. He got up on his elbow, began to swear at the other man, and promptly died.

Similar incidents can be observed in every practice. Dr. Wearn has a file that must be a foot thick. His friends have sent him all kinds of them: persons who die suddenly while attending a ball game, such as the opening kickoff of a football game; when they hold seven aces in pinochle (I think it is seven that are allowable), or when they get a royal straight flush. The excitement is too much for them and they keel over.

Another interesting point is the frequency with which a coronary occlusion occurs at night when a patient is at rest, you might say. And yet it is surprising how often dreams of a very exciting nature occur at the same time, apparently, as the coronary attack. I will cite a couple of examples.

A man who loved to hunt ducks had on his hip boots, in his dream, and was out hunting with his wife in a small boat. The boat became stuck. He got out, waded, and pushed his wife ahead of him in the boat. The going got tougher and he walked with greater and greater difficulty and effort. In the dream he felt himself becoming very short of breath and finally was in great pain. He awoke with a coronary occlusion.

Another man, in his dream, was going to the railroad station with his wife. They were to catch a train. His wife got on the train first, and he was held up in some way. The train was pulling out and he began to run to overtake it. As he ran, obstacle after obstacle got in his way. He became very short of breath, had chest pain and awoke with a coronary occlusion.

You can find such examples in your own practice if you question persons with heart disease carefully. It is a mistake to think that persons are at rest at night. Frequently they are far from it. Just being in bed does not necessarily put one at rest.

I don't mean to suggest that I think the dream brought on the coronary occlusion. I think it might have been one factor that did. I think also that it might be that the beginning coronary occlusion already had taken place and that in response to the pain the patient had the dream. It is extremely difficult to decide scientifically which comes first in such an instance. We know the rapidity with which dreams can take place. And dreams, you might say, also can be somewhat retroactive. A simple example is the alarm clock dream in which the alarm rings; if you don't want to get up, you dream a beautiful explanation of why you needn't get up, and you don't. On the other hand I think it is not unwise to consider the possibility that the excitement in the dreams I described might have had a good deal to do with the bringing on of the coronary spasms or coronary occlusions.

There is yet another facet to this which perhaps lends some credence. I have had an opportunity to study in detail 3 or 4 patients with known coronary disease. I first became interested in the first case when Dr. Harold Feil had a patient, a man about 57 years old, who had had a mild coronary occlusion and subsequently experienced paroxysmal auricular fibrillation. Dr. Feil was not impressed with the emotional aspects in this case, nor

was I, and it was the patient who insisted that he see a psychiatrist. I took him on most reluctantly and skeptically, telling Dr. Feil that I was sure I couldn't do anything in this instance and for heaven's sake not to get up any false hopes.

The man was a very successful person who for the past four years had been practically an invalid. He spent 10 days out of every month in bed, crippled by these attacks. He also had a very restricted working day when he did work. He insisted on seeing me because he found his relationship to his brother, with whom he worked, very upsetting. On his first visit he began by relating incidents which had occurred when he was a child. This, incidentally, was remarkable—to have a man walk into your office, especially one who pounds on your door to get in, sit right down and begin, "When I was 4 years old . . ." and then go right on from there.

His problem was this. He had the difficulty, as do so many people in our society, that he was not free in his thinking and in his feeling. His brother was the type who would have annoyed any one of us, but he was his brother, and it would have been very awkward to get him out of the business in a smooth and simple way. In other words, he was stuck with him. The patient was not free to express within himself the angry feelings that arose when his brother gave him cause.

I saw him once a week for about four months. I told him that he didn't choose his brother, to begin with; that it is perfectly normal, usually, for all of us to have a lot of anger and hostility toward people we love (sometimes we don't love them quite so much, but that was a tactful way of putting it), and I got him to let his thoughts come into his own mind and to express them—not to act them out by telling his brother what he thought of him, but to let them come into his own mind in clear fashion. These thoughts became extremely clear and definite.

Now, three years later, he is working 18 hours a day and really doing extremely well. And he doesn't go to bed any more—I mean during the day. The freedom he achieved to let his anger come out directly in his own mind seems to have been the factor that freed him from his attacks. Bottled-up anger, often bottled-up sexual drive, isn't safe, and it takes an underground route of expression if we don't let it out at least in our own minds. One doesn't have to act these things out, although sometimes that helps, but one does have to be frank in recognizing one's own feelings.

Two other patients, one woman and one man, both had coronary occlusion and very severe angina. An internist sent these 2 persons to us, and again it was with the greatest trepidation that we took them on. Treating somebody with an illness of this sort psychiatrically is quite a burden, because if a patient begins to tell you about those things which are important to him, he is likely to have a great deal of feeling in the telling. And when he has a great deal of feeling, he is very apt to have, certainly at the beginning, severe coronary spasms. This may frighten you, but you mustn't show it. When he is trying to hold something back he may have severe chest pain, which may disappear as soon as he tells you what is on his mind. If he expresses it with considerable freedom, pain may accompany this expression also.

We discussed this with the internist and said, "Look, we don't want this person to die on the couch, and we may well accomplish just that if we keep on going." The internist assured us that the patient might just as well die in our office as anywhere else and told us to go ahead. So we did.

In these 2 cases there have been excellent results, and by and large the story is the same as in the first—i.e., when these patients became freer in their thinking and in their feelings (and one of them particularly became quite free in the expression of her feelings—which has been a little tough on her husband but better for her heart), they both did remarkably well. Their anginal attacks have been almost entirely eradicated, although they still have them occasionally.

I think it is extremely important that all of you who see illnesses of this type pay some attention to this kind of approach. I think it will help you in the treatment of your patients, and I think it will help all of us who

are interested in pushing science ahead, if we can collect all kinds of data and perhaps point the way to how these attacks come about. One might think that the dammed-up emotional impulses come down over the vagus and exert their influence that way. But this is extremely difficult to prove, and one wonders.

Certainly it may well be that in excitement or anger the heart's action is greatly speeded up, perhaps just for a few minutes, and that its action out-demands the supply which the coronaries, already somewhat damaged by atherosclerosis or something similar, can deliver, so that there is a momentary, or perhaps not quite so momentary, deficit which gives rise to the pain. This, I think, is the ordinary explanation and certainly not a silly one.

It is interesting that stimulation of the hypothalamus in animals causes a marked increase in the work of the heart. However, no one has been able to find any mechanism that can switch the coronary arteries. So it seems most reasonable, in our present state of knowledge, to accept the hypothesis that the heart's work outgrows the supply of blood and that this discrepancy is perhaps the reason for the pain.

My feeling is that this is not the whole story—that there is a lot more to be learned. It seems, too, that the effects are often so quick that they are a little hard to explain.

It is also difficult to understand why so many persons with angina or with real occlusion are able to make sudden little exertions which, to my mind, certainly speed up the work of the heart a good deal, and yet they don't suffer any pain at that time. I think one is constantly surprised, if one takes a detailed history without prejudice, because so many of our preconceptions don't fit these patients. One patient can do one thing, and another patient another, with apparently complete impunity. Yet there are certain vulnerable spots, often spots in which particular and peculiar emotional feelings are involved, which are literally death for that patient.

MEETINGS AND POSTGRADUATE COURSES

La Rabida Sanitarium, Chicago: First annual institute in the field of rheumatic fever, beginning October 12 and continuing for five days. Conducted by members of the staff together with others selected from Chicago medical schools, the institute will be directed primarily to general practitioners and to nurses, medical social workers, occupational therapists and others interested in rheumatic fever and rheumatic heart disease. On October 16 the Gertrude F. Pick Memorial Center will be dedicated, and also on that day a lecture in memory of Dr. Robert A. Black will be inaugurated. For further information, write the Institute, La Rabida Sanitarium, East 65th Street and South Shore Drive, Chicago 49, Illinois.

Rheumatic Disease Congress, Geneva, Switzerland: The eighth International Congress of Rheumatic Diseases will be held August 24-28, 1953 at Geneva, Switzerland, with sessions also at Aix-les-Bains and Zurich. The meeting is sponsored by the International League Against Rheumatism. Presiding will be Professor E. Jarlov of Copenhagen. Further information may be obtained from Professor K. M. Walthard, Institut de Physiatrie, Cantonal Hospital, Geneva, Switzerland (cable address: Rheumatisme Genève). Travel information and reservations may be obtained from any American Express Company office.

Duke University School of Medicine, Durham, North Carolina: A month's course in medical mycology will be offered from July 1-29, 1953. The course, which will be under the direction of Dr. Norman F. Conant, will be offered every day in the week except Sunday. Inquiries should be directed to Dr. Conant.

Vagotomy in the Treatment of Peptic Ulcer

PAUL BANZET*

L'Hôpital Broussais, Paris, France

Although vagotomy has a very efficient action on peptic ulcer of the stomach or duodenum, I do not use it as a routine procedure in normal cases. I prefer gastrectomies which give me very satisfactory results. I do vagotomy in some selected cases: (1) recurrent ulcer after a previous operation, (2) duodenal ulcer, very far to the right, when removal could be dangerous for the common duct. Either procedure is followed by a gastroenterostomy.

PAUL BANZET

WHEN I was in the United States in 1946, the first reports by Dr. Lester Dragstedt on the results of vagotomy in treatment of ulcer were just being published. I was very interested in the procedure and went to see Dr. Dragstedt. We are now very good friends.

I would like to describe 3 interesting cases in which vagotomy was done. The first patient, a 42 year old man, underwent surgery because of a duodenal ulcer while he was in North Africa; the operation consisted of a gastroenterostomy. After a few months a peptic ulcer of the stoma developed. Another surgeon did a gastrectomy, removing a small section of the stomach and implanting the end of the stomach into the side of the jejunum (Polya operation) on a very long loop, on which he added an enteroenterostomy. This is a good procedure in experimental surgery when you want to create a peptic ulcer! So it was not surprising that another peptic ulcer developed three months after the second operation.

I operated on this man six months later. I found two large peptic ulcers, one at each end of the stoma. I did an extensive resection of the stomach and of the anastomotic loop, and made an end to end anastomosis on the small bowel. The anastomosis between stomach and bowel was a retrocolic Hofmeister type of stoma.

Following this operation the man was free from pain, but shortly thereafter he began to suffer again. I reoperated on him, about six months after the third surgical procedure, and found a recurrent ulcer of the stoma. I did another resection of the stomach and of the small bowel, an end to end anastomosis and another anastomosis between the stomach and the jejunum.

The patient was well for one month, after which time I was obliged to reoperate immediately because I thought he might have a gastrocolic fistula. I found a recurrent ulcer with a colonic perforation. I did another resection of the stomach, leaving only a very small portion, resected the jejunum again, and made an end to end anastomosis on the bowel. The

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Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

colonic perforation was sutured in three layers. The remaining portion of the stomach was so small that I made an anastomosis of the Polya type.

After this operation, which was a subtotal gastrectomy, this man was well and I thought he was cured. Then in 1946, while I was in this country, I received a cablegram from him which read: "New ulcer. Try to find something." When I returned to Paris he rushed into my office and asked if I had found something. I told him, "Yes, I will cut your vagus nerves." I did a vagotomy, but I wanted to see what was happening so I used an abdominal approach; as a result, this was the sixth operation the patient had undergone. At operation I found a peptic ulcer. I located the posterior right vagus nerve very easily, but I wasn't sure of the left one. All the same, the result was excellent and the patient was well for 18 months. Then he came to see me. He was a pitiful sight; he had lost a great deal of weight and was having two or three injections of morphine a day for relief of pain. He asked, "Well, what now can you do for me?" I told him, "I don't know. You have very little stomach left; I have cut your vagus nerves. Of course, I could do a total gastrectomy, which would be difficult but feasible. But I am not sure you would not have a recurrent ulcer on the esophagus. If you agree, I would like to open your chest and see how your vagus nerves are." He agreed. I opened his chest and found that the right vagus nerve had the appearance of an old string that could be torn by pulling it, but the left vagus nerve was in excellent condition. So I resected both vagus nerves.

Pathologic examination of the resected specimen showed the right vagus nerve to be completely degenerated, but the left vagus nerve was intact. The patient has been completely well for five years since resection of the vagus nerves. He has resumed his work and has no abdominal complaints.

This case illustrates (1) that vagotomy acts on the ulcer and (2) that some failures might be due to incomplete section of one of the vagus nerves. I have performed many vagotomies and have found that the right vagus nerve is always easily located but that this is not always true of the left one.

The second case also had its beginning in 1946. I had just returned to Paris from the United States. An excellent surgeon who lives outside of Paris and who does a great deal of gastric surgery came to me and said, "I am very embarrassed because six weeks ago I operated on a young man of 26 who had a duodenal ulcer. I made a simple large resection and eight days after the operation he began to suffer. He has six injections of morphine a day and he can't eat. What do you propose?" I told him that I thought I would try a vagotomy, and when I operated on the young man I found a huge peptic ulcer of the stoma with an inflammatory reaction which included the stomach, the mesentery, the mesocolon, the small bowel and the colon. It was impossible to do a direct operation on such a lesion, and if I had done another gastrectomy I am sure the result would have been fatal. So I did a vagus section.

As is usual in these cases, the next day the patient required no morphine and since then he has been perfectly well—it is now six years since vagotomy was done.

The third case is that of a patient whom I saw for the first time this year. One morning I came to the hospital and my residents told me that during the night a man with a perforated ulcer had been admitted. A suction tube had been placed in his stomach. The patient presented all the signs of perforated ulcer. I do not especially favor use of suction in cases of perforated ulcer. I told my residents to operate on this man, saying (and I don't know why), "I am not sure it is a perforation of the stomach." The next day they told me they had found a perforation not on the stomach but on one of the first jejunal loops (a rare occurrence), and they had sutured this perforation.

The man was discharged from the hospital 10 days later. In about six weeks he returned, complaining of severe epigastric pain. He was admitted, and the next morning my residents told me he had another perforation and that a suction tube had again been placed in the abdomen. Again the patient presented all

the signs of an acute perforation and I told my assistant to operate immediately. He found a perforated gastric ulcer, and the resident who had performed the previous operation told me he was certain the stomach had been seen intact six weeks earlier, with no signs of ulcer. This second perforation was sutured and the patient was discharged.

Two months later he came back, again complaining of severe pain. His protein level was very low; he had lost a great deal of weight, and he told me, "I suffer exactly the same way as I suffered before my perforations." The next day I operated on him and found two enormous callous ulcers, one on the stomach and one on the jejunum, and an extensive inflammatory reaction with huge glands in the mesentery. In this case, also, it would have been very difficult to do a direct operation; I would have had to remove a very large portion of the stomach and a very long section of the small bowel because of the jejunal ulcer. So I did a vagotomy and an anterior gastroenterostomy on a long loop.

This man has done very well and has been free from pain. I saw him a couple of months ago and he was in good condition.

A month ago I saw Dr. Dragstedt in Chicago and I told him about these 3 cases. He asked me, "Why, if you have had such good results, don't you do vagotomy in all cases of ulcer?" That is the point I am going to discuss. First of all, I don't perform vagotomy in all cases of ulcer because even though there have been very good results in some cases, many of them have presented certain inconveniences. In my first cases I did vagotomy without gastroenterostomy, surely a wrong procedure, with immediate dilatation of the stomach. Even with gastroenterostomy there often was distention of the bowel, with pain and diarrhea that was difficult to control.

Second, when you do a vagotomy and section the vagus nerves just below the diaphragm, you find two nerves which have branches to the stomach and to the pancreas, the liver, the small bowel and the colon. Is it harmless to cut those nerves? I don't know.

Third, and most important, it is admitted that when you do a vagotomy you must add a gastroenterostomy. I remember, about 30 or 35 years ago, when gastroenterostomy was the only surgical treatment for ulcer. This operation gave good results in 50 or 60 per cent of cases and was considered a good procedure. We have had to wait a long time—5, 10, 15 or 20 years—to observe recurrences of stomal ulcers which are sometimes so difficult to manage. They are impossible to cure by medical treatment. Another operation is required, and these operations are often difficult because of colonic perforations and deep adhesions. We have had to wait a long time to realize that gastroenterostomy is not the answer to peptic ulcer of the duodenum or the stomach.

Actually, when you do a vagotomy plus a gastroenterostomy you perform two operations, both of which have an action on the ulcer. You can't be sure, therefore, which has produced the effect, the vagotomy or the gastroenterostomy.

Also, when you perform a gastroenterostomy you say, "Well, I won't see any peptic ulcer because I have cut the vagus nerve." That is possible, but who can say what will happen in 5. 10 or 15 years? When organic nerves have been cut, it is difficult to predict what will happen. That is the most important reason I don't do vagotomy in normal cases of duodenal or gastric ulcer.

Another reason is that I do gastrectomies, and I am quite satisfied with the results of this procedure. I have performed this operation in about 3000 cases, and think it is a good method of surgical treatment of ulcer in cases which do not respond to good medical management. The immediate mortality rate is low, about 1 per cent, so it is not a dangerous procedure, and the functional results are excellent. About 85 per cent of my patients have had excellent results—they eat normally, return to their former jobs and are entirely satisfied.

One factor which prompts me to say that the majority of my patients are satisfied with their results is that about 60 per cent of them come to me directly and are not referred by other physicians; they are always sent by other patients I have operated on—proof that the

latter have had satisfactory results.

Of course, recurrences are observed following gastrectomy, but if the operation has been well done these are rare.

A few principles which must be observed in regard to gastrectomy are the following: (1) To avoid a high postoperative mortality rate you must be careful in closing the duodenal stump; I am convinced that nearly all deaths following gastrectomy are due to duodenal leakage. (2) The gastric resection must be sufficiently extensive to remove all the acid part of the stomach. I consider three-fourths the proper portion to resect, but you must not remove more than that. In France, Belgium, Holland and Switzerland I have noted instances in which surgeons have removed too much of the stomach—three-fourths is not eight-ninths or nine-tenths. Too extensive resection may be a cause of the dumping syndrome we hear so much about, and it also increases the chance of postoperative nutritional trouble. (3) The method of suture is very important. I have always used the procedure I call an "edge to edge" suture: two layers of continuous sutures with catgut, one taking only the mucosa and the other the muscle and serosa.

There have been some recurrences of ulcer in my series of patients who underwent gastrectomy, but these have been few in number. Perhaps some patients have been reoperated on by other surgeons; I personally have seen a great number of patients who have had recurrences of their ulcers following gastrectomies done elsewhere. In all those cases I have found some defect in the method in which operation was done to explain the recurrence: section of the stomach close to the pylorus; insufficient resection of the stomach; poor anastomosis; too small and rigid stoma, and other reasons.

I believe the foregoing explains why I prefer an operation which gives good results and why I do not want to utilize a procedure which, though efficient, causes doubt in my mind as to the status of the patient in 15 or 20 years. All the same, vagotomy is a remarkable procedure and is indicated in a certain number of selected cases; these are as follows:

1. Recurrences following gastrectomy or gastroenterostomy. In such a case, if the operation has been done well, I only cut the vagus nerves. If the operation has not been done well, I tend to make another resection, this time correctly, and always follow the resection with a vagotomy.

2. Stomal ulcer following gastroenterostomy. In such instances I usually do a gastrectomy, eventually a jejunectomy and lastly a vagotomy.

3. Very difficult duodenal ulcers. I almost always remove a duodenal ulcer, but in some cases it is situated so far to the right with such a degree of infiltration of the gastrohepatic ligament that there is danger of injury to the common duct. I used to open the common duct and put in a catheter in order to make a safe dissection, but now I no longer try to do a gastrectomy but do vagotomy plus gastroenterostomy.

I will never do a vagotomy in a case of gastric ulcer, because I believe there is a real danger of carcinoma when the ulcer is located on the lesser curvature. No one can be sure that a lesion on the lesser curvature of the stomach is not a carcinoma. A very interesting case of gastric ulcer was that of a man on whom I operated 17 years ago. The gastric lesion had all the features of an ulcer, and the pathologist told me it was an ulcer. The patient did very well. Fifteen years later he came to me one morning and said, "I am all right, but this morning I coughed and spit some blood." He brought me his handkerchief, in which was a small piece of tissue. I sent the piece of tissue to the pathologist, whose report was as follows: "Carcinoma of the lung; surely a metastasis of a digestive carcinoma." I showed the first pathologic report to him and he said, "That was not an ulcer; it was a carcinoma. The carcinomatous cells are the same in the stomach and in the lung."

I have explained my viewpoints on the subject of peptic ulcer. I am too old to change and I hope the future will show me I was right.

Surgical Treatment of Osteoarthritis of the Hip

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If we live long enough our hip joints will show wear and tear changes which will be diagnosed osteoarthritis. Joints which have been damaged by injury or disease, and those presenting a faulty articulation following Legg-Calvé-Perthes disease, slipped femoral epiphysis, or subluxation of the hip may develop osteoarthritis before the age of 40. For many of these patients a very satisfactory result can be obtained by an arthroplasty in which the deformed femoral head is replaced with a prosthesis made of VITALLIUM® *or stainless steel.*

EDWARD L. COMPERE

OSTEOARTHRITIS of the hip is more common than most physicians realize. The longer we live the more likely we are to have changes within our hip joints characterized by loss or fibrillation of the articular cartilage and proliferation of sclerotic bone on both sides of the joint and at the margins, a condition which produces loss of motion and at times knifelike pain.

Etiology

The etiologic factors may be multiple and varied, and include all conditions which result in a poor articulation. Inadequate acetabulum; subluxation; congenital dislocation which has been reduced but in which therapy was continued for an insufficient period of time to obtain depth and a smooth articulation approximating normal; subclinical (often unrecognized) or definite Legg-Calvé-Perthes disease of the hip—osteochondritis, as it is sometimes called; slipping of a capital epiphysis of the femur occurring during adolescence; dietary factors; injury other than slipping of the epiphysis; disease such as pyarthrosis during childhood, and heredity—all may influence the degenerative joint changes which eventually become diagnosed osteoarthritis.

Osteoarthritis of the hip is as much a part of the aging process as graying of the hair, wrinkling of the skin, or arteriosclerosis. Just as with graying of the hair, in some persons the process manifests itself early in life, in others late. Osteoarthritis of the hip has been found in the mummies of ancient Egypt and in the skeletons removed from Indian mounds of both North and South America. It affects four-footed animals as well as human beings.

The minimal traumas of everyday life, the wear and tear of everyday activities, have their effect on weight-bearing joints to a greater extent than on others. Any articulation which is less than perfect will "burn out" much earlier than will one which functions

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perfectly. That is why subluxation, congenital dislocation, Legg-Calvé-Perthes disease and slipped femoral epiphysis, each leaving deformity within the hip, are so important as etiologic factors. In my opinion the vast majority of those persons who begin to have hip joint symptoms before the age of 50 years have had less than a perfect articulation from adolescence if not from birth.

Treatment

Through the decades of your experience and mine, treatment of osteoarthritis of the hip has varied, but no specific method has resulted. We cannot reverse the effects of wear and tear or the aging processes.

Nonsurgical therapy has consisted principally of rest, and this still is one of the most important ways of dealing with the problem. If a person who has symptoms of osteoarthritis and whose roentgenograms show beginning changes indicative of the wear and tear processes is willing to reorganize his life—to give up golf, avoid walking when he can ride, etc.—he may prolong the usefulness of his hip joint and delay disability for many years. Rest in bed with traction often has relieved the acutely painful hip, providing a degree of comfort and activity for months or years. Crutches have been advised. Heat and massage, because of the benefit to the local circulation, and salicylates, because of their aid in diminishing the discomfort, have proved valuable.

Today we have a new drug, BUTAZOLIDIN®. This product, however, has not been prescribed without some degree of risk. Given in doses originally recommended, it may produce dangerous blood changes, and yet this is the one drug I have found which actually relieves pain of osteoarthritis. Given in smaller doses, it has not been found to produce the damage to the hematopoietic tissues that has been described with larger doses.

ACTH and cortisone are of little value in osteoarthritis of the hip. An increase in the dietary protein intake, and AMIGEN®, amino acids and other protein concentrates given intravenously and orally have appeared to be of greater value than ACTH or cortisone.

In many instances of osteoarthritis of the hip we are faced with the necessity for more direct treatment. Surgical procedures of various kinds have been performed, with varying degrees of success. For the osteoarthritic hip which has become truly disabling, arthrodesis has perhaps given the greatest degree of relief from pain. It does have the disadvantage that it results in loss of motion, but a stiff hip in good position is far less disabling than most physicians realize. Many patients refuse to have an arthrodesis; they prefer some discomfort with preserved hip motion.

Acetabuloplasty, as recommended by Smith-Petersen, with removal of the overhanging osteophytic bone around the acetabulum and of the thick and edematous capsule, has afforded a greater degree of relief to some patients than to others. Such benefit as accrued from acetabuloplasty, or from so-called debridement—cleaning out of the joint and trying to trim off the rough surfaces and osteophytes as recommended by Magnusson—probably was the result of denervation. The excision of the joint capsule removed much of the nerve supply of the anterior and superior portions of the joint. The patient still had his arthritis and limitation of motion, and pain recurred.

Subtrochanteric osteotomy, which makes it possible to shift a new weight-bearing surface to the top weight-bearing position of the femoral head—a surface that has not been worn down as much as that on which the patient has been walking—also has proved helpful.

Within recent years, beginning in 1936 and 1937 when Smith-Petersen did his first work with the vitallium cup, arthroplasties of the hip have been more successful in relieving pain and maintaining a degree of motion than the other procedures mentioned, and as a result they have become widely used. Before Smith-Petersen's vitallium cup, occasional arthroplasties of the hip were done, using other substances to prevent refusion of the hip. These substances included pig bladder, used by Baer in Baltimore, and fascia lata to cover the head of the femur, used by many surgeons throughout the United States.

Unfortunately, even in the hands of such

an expert worker as Smith-Petersen himself, many cup arthroplasties did not stand up. Bone grew around the edges of the cup, or the edge of the cup cut into the neck of the femur and produced irritative inflammation and pain. In many cases the arthroplasty had to be revised, some of them two or three times, and finally some patients requested arthrodesis.

Some patients who were not considered good risks or who for other reasons could not be subjected to arthroplasty were treated by denervation. The obturator nerve can be completely severed intrapelvically, or the anterior branches which most often carry nerve supply to the hip joint and also innervate the adductor muscles may be avulsed at the same time that the tight adductors are released by tenotomy.

Excision of the sciatic nerve branch to the hip joint or of the femoral nerve branch is not so easy. Sometimes the nerve branches are difficult to find. Also, experience has shown that even when all nerve branches that can be found are severed, relief of pain for more than a few weeks is not obtained in at least 50 per cent of cases. Combined with arthroplasty, section of tight adductor muscles and avulsion of the anterior obturator nerve are worth while.

Within recent years we have had a new armamentarium made available to us which seems to offer a better answer to the treatment of osteoarthritis of the hip in cases in which major surgery is justified. Two brothers, Robert and Jean Judet of Paris, were the first to present a large series of patients in whom the deformed and arthritic femoral heads had been replaced with ones made of acrylic. Since that time modifications of the prosthesis have been developed, and these now number more than 100. Most of them are of four different materials: acrylic, NYLON®, vitallium and stainless steel. I prefer stainless steel, but surgeons in various parts of the country have reported excellent results regardless of the material used. The acrylic femoral heads in some instances have become brittle and have broken within the hip joint. Acrylic does not cast a shadow in the roentgenogram, and sometimes the only way to determine the reason for severe pain is to reinvade the hip joint. In most such instances we have found a split-off portion of the acrylic head. Nylon is a tougher substance and is more resilient, but it has a tendency to tighten in the hip joint. Vitallium is more brittle than stainless steel and the stem must be much thicker to provide reasonable assurance that it will not break.

Regardless of age, if heart and renal function appears satisfactory for an operation, patients will withstand this type of surgery quite well. Formerly we were afraid to operate on older persons for fear there would be a surgical death. We have operated successfully on patients more than 90 years of age and there have been no operative deaths.

The posterolateral approach is used for several reasons. Patients who have had the hip joint capsule opened posteriorly do not subsequently dislocate the prosthesis, while dislocations have occurred in cases in which the anterior approach was used.

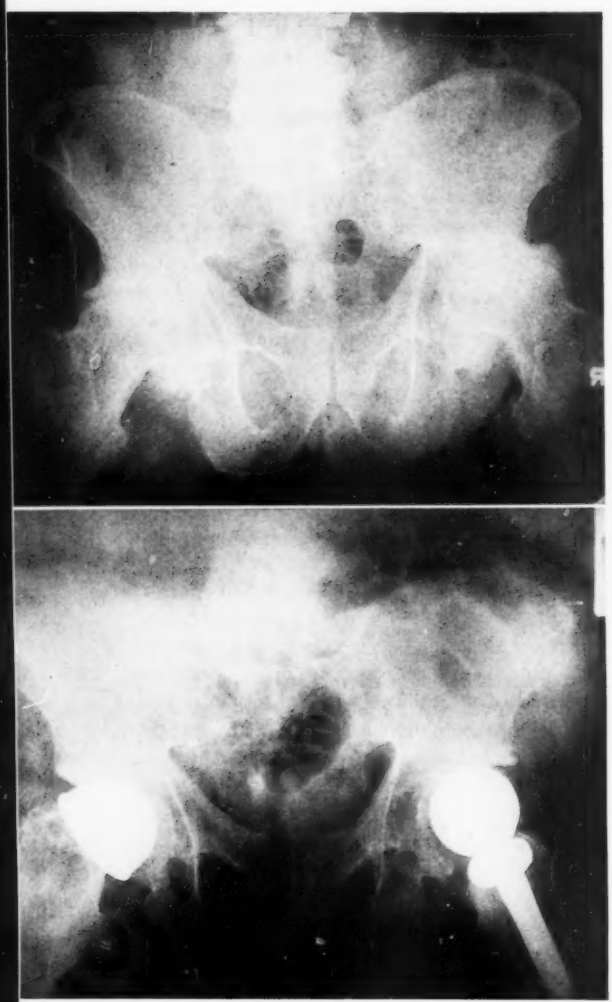
Case Reports

A 32 year old woman, the daughter of a physician, came to me because of severe pain in her hip. It was impossible for her to carry on her housework. I did a fusion of the hip in 1938 and she has had good function without pain since that time. Recently she came to me because the other hip had become very painful. I intend to use an Eicher stainless steel prosthesis for repair of this hip.

A 35 year old woman whom I had seen in consultation was operated on by another physician, against my advice. She had subluxation and a very painful hip. The operation consisted of a vitallium cup arthroplasty, and the patient never was able to bear any weight on the hip following the procedure. Any motion produced pain. The acetabulum was not deep enough and the cup was very close to the neck of the femur. I removed the cup and did an arthrodesis. In such a case today I probably would use a prosthesis if the patient would permit me to do so, but she had had so much pain and had been told so often that a stiff hip would be painless that she preferred

FIGURE 1. Extensive osteoarthritis with partial collapse of both femoral heads in a 76 year old man. Motion was limited to a few degrees. The lower roentgenogram shows the appearance of the hips following vitallium cup arthroplasty of the one and Eicher prosthesis arthroplasty of the other. The hip with the vitallium cup has a greater range of motion and less discomfort than does the hip in which the prosthesis was used.

FIGURE 2. Roentgenogram of the hip of a 64 year old man showing aseptic necrosis following open reduction and bone graft because of a nonunited fracture. Osteoarthritis is also present in this hip. The lower roentgenogram was taken following removal of the necrotic femoral head and insertion of an Eicher prosthesis. This patient has obtained a good result, with a joint which approximates normal.



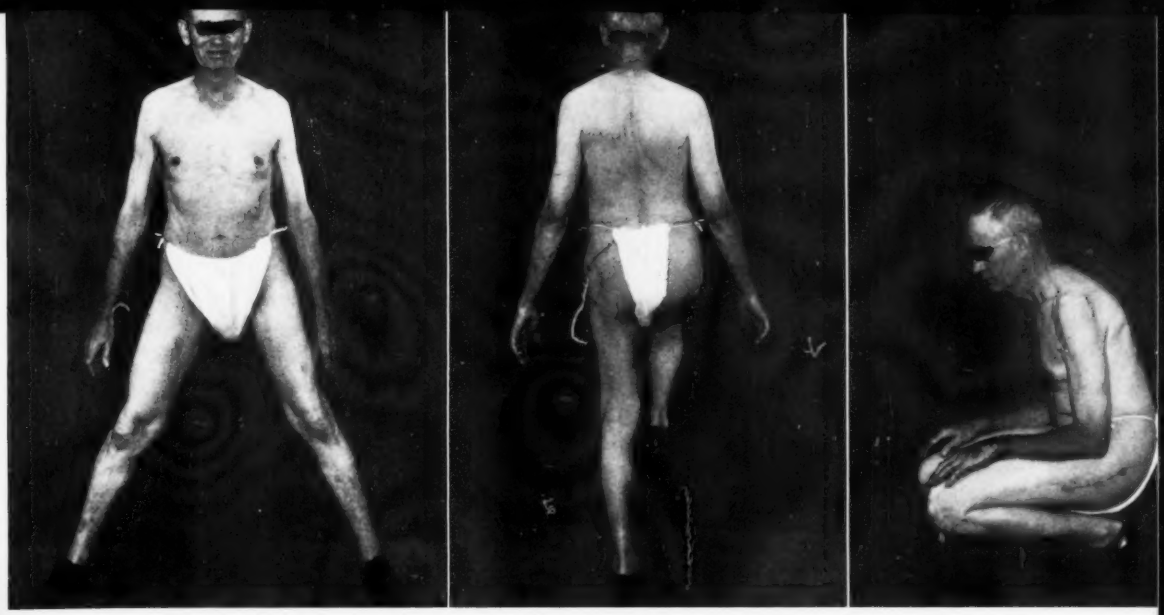


FIGURE 3. Same patient as in Figure 2. Four and one-half months after operation, motion is slightly limited in abduction but is otherwise normal. The patient has no pain and is working as a carpenter. He had not been able to work at his trade for 18 months before insertion of the prosthesis.

it. She is very happy with the result.

A very large man, a gardener of Swedish ancestry, came to me because his hip had become very painful and he was unable to do his work. He was very concerned that he might never be able to work again. I used the Judet acrylic prosthesis, the only type available at that time. The prosthesis had a steel stem, and small pins were used to reattach the trochanters. Now I do not remove the trochanter, but merely detach the muscles, leaving a little bit of the tendon, and resuture them subsequently. This man has continued to do heavy work. This is one case in which the acrylic prosthesis has stood up. The stem has not loosened where it enters the cortex.

A 76 year old man who had been active all his life had such painful hips that he could barely walk. He owns a small real estate and insurance business. During years of treatment he had had intrapelvic neurectomies of both obturator nerves, with temporary relief of pain. He had been hospitalized many times, and traction and other conservative measures had been employed, but he finally realized that he must give up all activity unless more adequate relief could be found. I decided to compare two types of procedures, and did a vitallium cup arthroplasty on one hip and an Eicher prosthesis arthroplasty on the other (Figure 1). There is a greater range of motion in the hip with the vitallium cup. The patient now carries on his business with very little discomfort, and is satisfied with the result.

A 64 year old man had osteoarthritis that developed following a fracture of the neck of the femur which had not united. A bone graft produced union but aseptic necrosis of the femoral head followed. This man, a carpenter, had not been able to work for 18 months. I inserted an Eicher stainless steel prosthesis, and within three months he was back at work, which included climbing ladders and building houses (Figure 2).

Photographs taken four and one-half months after operation are shown in Figure 3. Motion is slightly limited in abduction but is otherwise normal. The Trendelenburg sign is negative, as is the case in nearly all the patients who have the Eicher prosthesis.

In my opinion the Eicher prosthesis is more likely to produce a good result than a vitallium cup arthroplasty. It is much too early to know what the final results will be, but in these older patients who do not have more than 10 or 15 years to live, the chance seems worth taking. In younger patients we may, at some future time, regret having put these prostheses in, and then we will have nothing to offer except arthrodesis.

Lesions of the Adrenal Glands of Surgical Significance

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Hyperfunction of the adrenal cortices caused either by hyperplasia or by functioning tumor results in a variety of recognizable clinical syndromes, most of which are amenable to surgical treatment. Others may respond favorably to medical management. Paroxysmal or persistent hypertension caused by functioning tumor of the medulla of the adrenal gland can be cured by surgical intervention in most cases.

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ROBERT M. SALASSA

In the human body few if any structures of similar size play a more significant role in the regulation of normal physiologic processes and various pathologic states than the adrenal glands. This fact is explained in part by the dual embryologic background of these glands. The cortex, which is of mesodermal origin, arises from cells near the mesonephron in close proximity with the primitive sex gland. As one might expect, therefore, two important products of cortical secretion are androgens and estrogens. In addition, the adrenal cortex produces other steroids, which are concerned with metabolism of protein, fat and carbohydrate as well as with retention of salt and water. In contrast, the medulla is derived of ectodermal tissue in close association with the site of origin of the sympathetic ganglion cells. The most important known secretions of the medulla are adrenalin and noradrenalin, both of which, in ordinary amounts, increase the systolic blood pressure.

A variety of disease states may be produced by abnormal function of the adrenal glands. Some of these can be recognized with considerable certainty at the present time, and it seems probable that more of them will be recognized in the future. Hypofunction of the adrenal cortices, resulting in Addison's disease, has long been recognized by the internist. Fortunately it can now be treated more effectively than in former years. The surgeon is concerned primarily with hyperfunction of the adrenal glands, caused either by hyperplasia of the cortex or by a functioning tumor of either the cortex or the medulla. He must be familiar, however, with the prevention and treatment of adrenal insufficiency as this state may occur after certain operations on the adrenal glands.

Tumors of the adrenal cortex are generally unilateral, functioning tumors which are either benign or of a relatively low grade

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type of malignancy, although nonfunctioning tumors of the adrenal cortex are not rare. In view of the many different products of adrenocortical secretion it is not surprising that clinical syndromes produced by functioning tumor of the adrenal cortex may vary considerably depending on the type and amount of secretory products which are produced as well as on the age and sex of the patient. Actually, hyperplasia of the adrenal cortices is a more common cause of cortical hyperfunction than is tumor. In contrast, hyperplasia of the adrenal medulla has not been recognized as a clinical entity, although functioning tumors of the medullary portion of the gland are well known.

Lesions of Adrenal Cortex

Less common manifestations—The adrenogenital syndrome is caused by excess secretion of androgens, and its clinical manifestations depend on the age and sex of the patient. Thus, congenital adrenocortical hyperplasia occurring between the third and fifth months of intrauterine life results in pseudohermaphroditism in girls at the time of birth. The clitoris is enlarged and other genital changes suggest bisexuality. Evidences of excessive androgenic activity persist and somatic precocity occurs as the child develops. Congenital adrenal hyperplasia occurring in males results in macrogenitosomia praecox (Wilkins[1]) with excessive genital development frequently being present at birth. Evidence of excessive androgenic activity persists after birth and both somatic and sexual precocity occur. However, the testes remain small and spermatogenesis does not occur. While congenital adrenocortical hyperplasia is characterized by evidences of excess androgenic activity in both the male and female infant, these same patients also may show evidences of adrenal (cortical) insufficiency associated with dehydration and loss of sodium and chloride.

The postnatal occurrence of adrenocortical hyperfunction, caused by either hyperplasia or functioning tumor in girls is characterized by normal appearance at birth with subsequent evidence of virilism and somatic precocity. The clitoris may become hypertrophied; early development of axillary and pubic hair is noted and premature closing of the epiphyses occurs accompanied by abnormal development of the muscles and by increased muscular strength. Virilism occurs when this syndrome develops in women. Amenorrhea, hirsutism, acne and a deep voice usually develop; the breasts atrophy and subcutaneous fat is lost.

Development of the adrenogenital syndrome postnatally in young boys results in somatic and homologous sexual precocity. The onset of this syndrome has not been recognized clinically in men. Attempts to control excessive androgenic activity associated with adrenocortical hyperplasia (either congenital or postnatal) by resection of the adrenals have not been successful. Wilkins observed that cortisone would decrease the excretion of 17-ketosteroids in the cases of adrenogenital syndrome associated with adrenocortical hyperplasia. It is hoped that the use of cortisone also will control the clinical manifestations of this condition.

Feminizing tumors of the adrenal cortex may occur in men, although they are uncommon. To our knowledge only 14 authentic cases of this type have been reported in the literature. We have seen 1 such patient from whom a large adrenocortical tumor was removed with an early result that appears to be satisfactory. In the female, 1 case has been reported of homologous sexual precocity in association with numerous adrenal cell rests scattered through the ovaries and over the peritoneum.

Mixed clinical pictures are encountered frequently. Tumors of the adrenal cortex may cause a single endocrine abnormality, such as diabetes, or they may be entirely nonfunctioning. In the latter instance presence of the tumor is known only by the existence of a gradually enlarging mass in the upper part of the abdomen on the right or left side and the pressure symptoms which such a lesion may produce.

Cushing's syndrome—Cushing's syndrome, which is probably the commonest clinical manifestation of excessive function of the ad-

FIGURE 1. Cushing's syndrome associated with adrenal hyperplasia. *a.* Prior to operation. Note roundness of face, obesity of neck, acne and hirsutism. *b.* Six months after subtotal adrenalectomy. Note return to normal appearance.

renal cortices caused by either hyperplasia or tumor, is seen most often in young women, but it also is encountered in men and less often in children. The general physical and cutaneous changes which are present when Cushing's syndrome is well developed make for easy recognition of the patient who suffers from this condition (Figures 1 and 2). Not all patients evidence pronounced changes, however, so that corroborative laboratory data are helpful.

Characteristically the patient with Cushing's syndrome shows a special type of obesity, manifested by a round, obese face (moon face); obesity of the neck and trunk, especially the abdomen, and a deposition of fat in the cervicodorsal region which has been termed "buffalo hump." The extremities actually may be wasted or at least appear so, in contrast with the trunk. Muscular weakness becomes increasingly severe. Associated cutaneous changes include mild to moderate degrees of hirsutism. Acne of some degree is usually present on the face and often over the back and chest. A plethoric complexion uniformly develops and becomes easily noticeable. Purplish striae develop over the abdomen and at times also on the thighs and upper parts of the arms. Ecchymoses form on the extremities and may be prominent. The skin becomes thin. Other changes may include amenorrhea in women and impotence in men. Hypertension of varying severity is noted and psychiatric changes of varying severity are not uncommon.

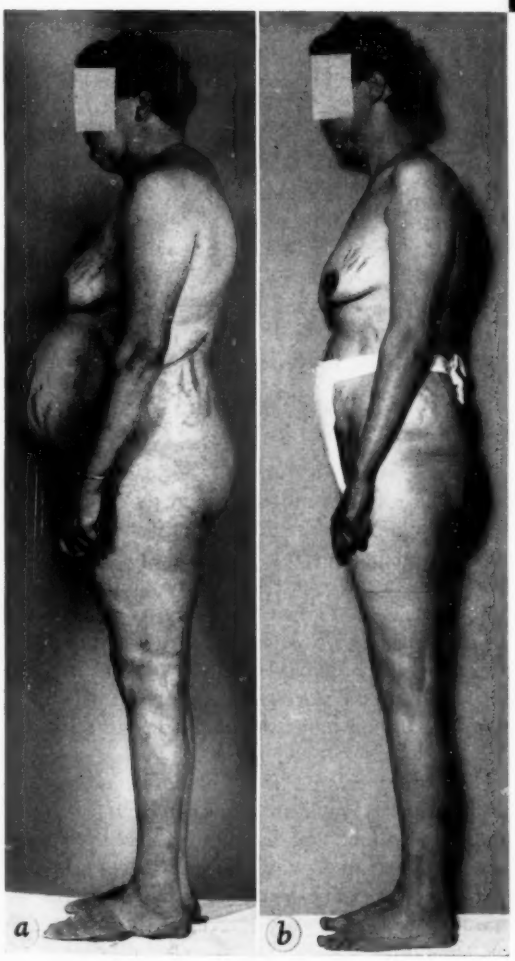
Significant laboratory findings include the following: lowered values for chlorides and potassium in the blood, alkalosis, lymphopenia, lowered tolerance for glucose, alkaline urine and an increased excretion of corticosteroids in the urine. Excretion of 17-ketosteroids in the urine may be high, normal or low. Osteoporosis is often present and may result in one or more spontaneous fractures.

Currently the treatment of Cushing's syndrome is more standardized than in former years. It is now realized that regardless of the basic etiologic factor in Cushing's syndrome the disease process is mediated through hyperfunction or abnormal function of the adrenal glands. Treatment consists of removing a functioning tumor, if present; if none is present, resection of an adequate amount of adrenal tissue is carried out so that symptoms of hyperfunction are relieved. It should be realized that usually it is now known prior to surgical exploration whether tumor or hyperfunction without tumor is responsible for the patient's symptoms. Thus, at the time of operation the surgeon must determine the path-

FIGURE 2 *(below)*. Same patient as in Figure 1. *a*. Prior to operation. Note deposition of fat in cervicodorsal region, obesity of trunk, striae over abdomen and ecchymoses of lower half of legs. *b*. Six months after subtotal adrenalectomy. Note return to normal appearance.

(Figures 1 and 2 reprinted from Priestley, J. T., Sprague, R. G., Walters, Waltman and Salassa, R. M.: Subtotal adrenalectomy for Cushing's syndrome: A preliminary report of 29 cases. Ann. Surg. 134:464-475 [September] 1951.)

FIGURE 3 *(right)*. Adrenocortical tumor. Pronounced atrophy of uninvolved portion of adrenal gland is evident.



ologic process responsible for the patient's symptoms. Usually this can be accomplished after some experience, without too much difficulty. This is true because fortunately if a functioning adrenocortical tumor is present in one adrenal gland, the opposite gland is always atrophic (Figure 3). In contrast, if hyperfunction is responsible for the patient's symptoms, the appearance of the adrenal glands is identical and neither is atrophic. Under these circumstances the adrenal glands may be of normal size and appearance but usually they are enlarged. Hyperfunctioning adrenal glands have been removed which are four times as heavy as a gland of normal size. Inasmuch as the patient with Cushing's syndrome is commonly obese, an anterior surgical approach is not employed. It is our practice to use bilateral posterolumbar incisions, closing the first incision and turning the patient to the other side before making the second incision.

Currently the surgical treatment of Cushing's syndrome is carried out in the following manner: If there is any evidence which suggests the presence of tumor on one side, the adrenal gland on the affected side is exposed first. If a tumor is found it is removed and no further operation is done. If, however, a tumor is not found on the first side and if this adrenal gland appears to be atrophic, the

incision is closed and the opposite adrenal is exposed with reasonable expectation of finding a tumor, which is then removed. If at the time the first adrenal gland is exposed, no tumor is found and the gland is not atrophic, it is considered (providing the surgeon is completely satisfied with the preoperative diagnosis) that hyperfunction is responsible for the patient's symptoms and approximately 85 to 90 per cent of the gland is removed. An attempt is always made to preserve an adequate supply of blood for the portion of gland which remains. The incision is then closed and total adrenalectomy is performed on the opposite side. Bilateral total adrenalectomy has been suggested as the treatment for Cushing's syndrome, but as yet we have employed this procedure only in the exceptional case. This point of view may change in the future.

Preoperative preparation and postoperative care are of greatest importance in the surgical treatment of Cushing's syndrome. Efforts should be made preoperatively to correct any electrolyte imbalance which exists. Preparations should always be made to prevent acute adrenal insufficiency which will occur immediately after operation if a functioning cortical tumor is removed, owing to the atrophy of disuse which exists in the remaining adrenal gland. In addition, if an extensive subtotal (85 to 90 per cent) resection of one adrenal gland is performed and total adrenalectomy is carried out on the opposite side, there is a possibility that an insufficient remnant of adrenal tissue has been preserved to prevent adrenal insufficiency or that an inadequate supply of blood has been maintained for this remnant. Cortisone is given preoperatively to obviate the possibility of postoperative adrenal insufficiency. It has been learned that a satisfactory practice is to administer 200 mg. of cortisone acetate intramuscularly 48 and 24 hours prior to operation and also the day of operation. As a rule cortisone is given postoperatively in decreasing doses. The condition of the patient determines the rate at which the dose of cortisone is reduced.

In many cases, after the surgical treatment just outlined, a delayed postoperative reaction will develop characterized by anorexia, nausea, vomiting, weakness, tachycardia, fever, moderate drop in blood pressure, inanition, loss of weight and perhaps abdominal pain or discomfort. Somewhat variable electrolytic changes may be noted in the blood during this period. The administration of cortisone will control this reaction. If a functioning tumor has been removed it is seldom necessary to continue the administration of cortisone for a prolonged period. However, for approximately half of the patients who have had extensive bilateral removal of adrenal tissue because of hyperplasia, as already outlined, it has been necessary to continue the administration of cortisone indefinitely after operation.

Results of the surgical treatment of Cushing's syndrome have been universally favorable if a functioning cortical tumor has been removed, provided the tumor was not malignant. Treatment of Cushing's syndrome due to hyperplasia has likewise been successful although incomplete remission or recurrence of symptoms has required reoperation in a small number of the earlier cases. Remission of the disease and return to health after operation require a variable period, which in general is proportionate to the severity of the disease and the duration of its preoperative existence.

Lesions of the Medulla

Various types of tumors can arise from the medulla of the adrenal gland. Neuroblastoma, a highly malignant tumor, is occasionally seen in children. The counterpart of this lesion in the adult is the ganglioneuroma which is less malignant and permits a more favorable prognosis. Another type is the pheochromocytoma, which is usually a functioning tumor of the adrenal gland. We wish to give this tumor more detailed consideration (Figure 4).

Clinical aspects—Pheochromocytoma may produce paroxysmal or persistent hypertension. The patient who has paroxysmal hypertension associated with pheochromocytoma commonly experiences attacks of hypertension characterized usually by several of the following symptoms: headache, anxiety, dizziness,

sweating, palpitation, pain in the thorax or abdomen, flushing or blanching of the face, nervousness and tremor. These attacks usually persist for only 10 to 15 minutes, but may last several days or even longer. In some cases pressure above a kidney may precipitate an attack. The patient who has persistent hypertension caused by pheochromocytoma may have a condition which clinically appears identical with essential hypertension. Associated attacks also may occur. The presence of a pheochromocytoma should always be suspected in children who have hypertension. It also should be suspected if the basal metabolic rate is elevated and tolerance for glucose is decreased in association with sustained hypertension.

Fortunately there are certain pharmacologic tests which are extremely helpful in the diagnosis of pheochromocytoma, although unfortunately none of these tests is infallible. In general these tests consist of the administration of certain drugs which may precipitate an attack of paroxysmal hypertension on the one hand or on the other hand may result in a pronounced fall in blood pressure if the patient has persistent hypertension caused by pheochromocytoma. In the former category histamine has given the most reliable results but tetraethylammonium chloride and methacholine chloride also have been used. In the latter category regitine has been more reliable but piperoxan hydrochloride and DIBENAMINE® also have been used. Unfortunately both false negative and false positive results have been obtained with each one of these pharmacologic agents. Care must be exercised in interpretation of results and tests should be repeated if results are equivocal. It seems reasonable to expect an occasional negative result from exploration for pheochromocytoma if certain of these tumors are not to be overlooked.

Surgical considerations—Appreciation of certain pathologic aspects of pheochromocytoma is essential in the proper surgical treatment of these tumors. It is true that usually a pheochromocytoma occurs as a single, benign unilateral tumor, situated in an adrenal gland. There are exceptions, however, as these tumors may be multiple, bilateral, malignant, or ectopic in location. Because of these possibilities it is necessary to explore both adrenals carefully in every case, even though a tumor

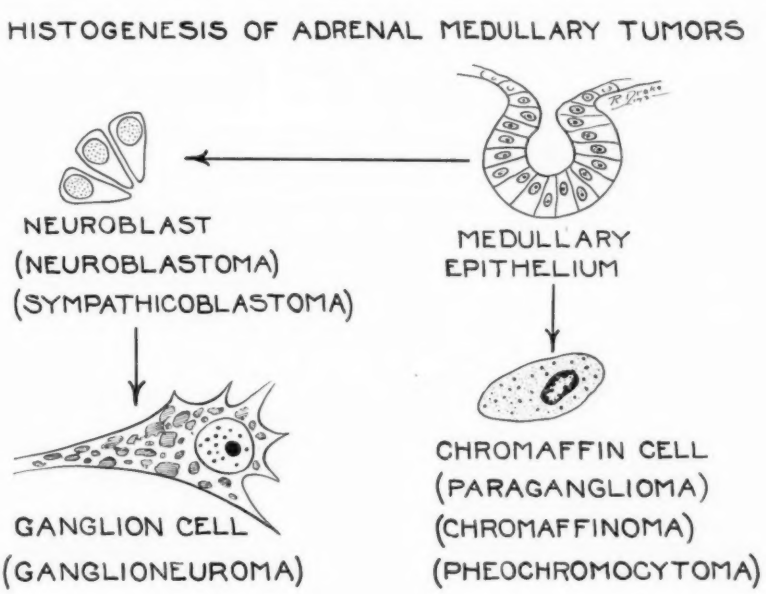


FIGURE 4. Histogenesis of adrenal medullary tumors.

(From Kvale, W. F., Roth, Grace M., Clagett, O. T. and Dockerty, M. B.: Headache and paroxysmal hypertension: Observations before and after the surgical removal of a pheochromocytoma. S. Clin. North America 24:922-933 [August] 1944.)

is found on exposure of the first gland, and it also is necessary to explore the abdomen in general and the retroperitoneal tissues along the aorta and the root of the mesentery in particular. Fortunately, patients who have a pheochromocytoma are uniformly thin, which facilitates an anterior approach through a transverse incision placed in the upper part of the abdomen. Such an incision readily permits careful exploration of the entire abdomen as well as the adrenal glands. If a tumor is not found in the abdomen, the possibility of one being located within the thorax or even the neck must be considered, providing the preoperative diagnosis appears to be correct. The surgeon need not fear postoperative adrenocortical insufficiency after removal of a pheochromocytoma such as occurs after removal of a functioning tumor of the adrenal cortex, although the blood pressure commonly needs to be supported, and for this reason preoperative preparation with cortisone is not necessary. If, however, bilateral tumors are removed from the adrenal glands and there is any question concerning whether or not it has been possible to preserve an adequate amount of adrenal tissue, vigorous measures to prevent the occurrence of acute adrenal insufficiency must be initiated.

Changes in blood pressure which occur during operation for pheochromocytoma require special consideration. Almost invariably there is an elevation of blood pressure as anesthesia is induced and the incision is made. In fact, if this does not occur the surgeon becomes doubtful of the actual presence of a pheochromocytoma. Palpation and manipulation of one of these tumors cause a precipitous rise in blood pressure, and therefore these maneuvers should be kept to a minimum. It is essential for the safe control of blood pressure during operation to have both pressor and depressor drugs available. Commonly the slow intravenous administration of dextrose is started as anesthesia is induced in order to facilitate prompt administration of drugs as desired. Regitine is most often employed to depress blood pressure if too great elevation occurs. Noradrenalin is employed to correct the pronounced hypotension which follows removal of the tumor. It is usually necessary to continue the administration of these agents, preferably by means of slow intravenous infusion, for several days postoperatively, especially if sustained hypertension existed preoperatively. If only paroxysmal hypertension occurred preoperatively, less prolonged administration is generally required.

Results of removal of pheochromocytoma are invariably good. Paroxysmal attacks are eliminated and persistent hypertension, if it has been present, is cured unless it has existed for so long preoperatively that secondary cardiovascular changes have occurred which do not permit complete return to normal. As a rule, if a malignant tumor is removed great improvement in the patient's condition may be expected for a long period of time if not permanently.

Other Conditions

Bilateral total adrenalectomy or unilateral total adrenalectomy associated with subtotal removal of the opposite adrenal gland has been employed in the treatment of essential hypertension. At present, these procedures are in the phase of clinical trial and evaluation. Further time will be required before their true efficacy and value become known. Since the work of Huggins and associates,[2,3] complete removal of both adrenal glands has been performed in selected cases of metastasis from carcinoma of the prostate and also carcinoma of the female or male breast. While experience with this procedure has been somewhat limited, there is evidence that in a certain percentage of these patients palliation has followed total adrenalectomy. More accurate evaluation of the indications and efficacy of this procedure will require still further observation.

REFERENCES

1. Wilkins, Lawson: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence. Springfield, Illinois, Charles C Thomas, 1950, 384 pp.
2. Huggins, Charles and Bergenstal, D. M.: Inhibition of human mammary and prostatic cancers by adrenalectomy. Cancer Research 12:134-141 (February) 1952.
3. Talalay, Paul, Takano, G. M. V. and Huggins, Charles: Studies on the Walker tumor. II. Effects of adrenalectomy and hypophysectomy on tumor growth in tube-fed rats. Cancer Research 12:838-843 (November) 1952.

Splenectomy for Blood Dyscrasias

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Splenectomy is a highly satisfactory form of therapy for the hypersplenic syndrome. An accurate definition of hypersplenism and a satisfactory understanding of this term are lacking at the present time. This article attempts to confine the term hypersplenism to a few well recognized syndromes and discusses some of the author's experiences with both the successful and unsuccessful use of splenectomy in the treatment of them.

WILLIAM D. HOLDEN

THE term "hypersplenism" is a vague word, and its definition is poorly understood by both practicing physicians and the various experts in the field of splenic disorders. For its clarification, it is perhaps best first to define "splenism," a term coined by Dr. Dameshek of Boston. He described splenism as a normal physiologic state in which a measure of control is exerted by the spleen over the rate of discharge of erythrocytes, granulocytes and thrombocytes from the bone marrow. This hormonal inhibitory control is evidenced by the almost routine response of the cellular elements of the bone marrow and the increased rate of discharge of these elements into the circulating blood following an incidental splenectomy. Further evidence is the gratifying response that occurs in occasional instances after splenectomy is done for congenital hypoplasia of the bone marrow—in other words, a condition in which the bone marrow is not producing the cellular elements as rapidly as it normally should.

Two theories exist concerning hypersplenism. The first is that the spleen is destroying unusual numbers of erythrocytes, granulocytes or platelets within the splenic pulp, that these cellular elements circulating in the blood stream are sequestrated, and that there is phagocytic activity by the splenic macrophages, which are destroying these cellular elements more rapidly than is normally observed; as a result of this sequestration and rapid phagocytic activity, the spleen usually will become enlarged.

The second theory, perhaps more generally accepted, concerns the hormonal relationship of the spleen to the bone marrow. According to this definition of hypersplenism there is interference by the spleen with the discharge of granulocytes and thrombocytes from the bone marrow. In other words, instead of there being a normal inhibitory control there is excessive inhibition of discharge from the bone marrow. Evidence of this interference is the extremely rapid response of bone marrow following splenectomy. Further evidence is the fact that if blood is taken from a person

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with idiopathic thrombocytopenic purpura, one of the hypersplenic syndromes, and given to a normal recipient, that recipient may develop thrombocytopenia, strongly suggesting that there is some circulating hormone or antibody that produces this inhibition of bone marrow activity.

Another bit of evidence is the fact that following removal of the spleen for thrombocytopenia, neutropenia or panhematopenia, the patient may be quite well for a varying length of time and then experience a recurrence that resembles the original syndrome. In some such instances an accessory spleen is found at exploration. These accessory spleens may measure no more than 1.5 to 2.5 cm. in diameter, and yet their removal will again produce a cure of the hypersplenic state. It is somewhat difficult to imagine a small organ of that sort exerting anything more than hormonal control over bone marrow discharge—that such a small spleen can phagocytize so many cells so rapidly that it produces this depression of circulating granulocytes and thrombocytes.

Among the various factors involved in diagnosis of hypersplenism is the size of the spleen. It is well known that in thrombocytopenia the spleen is not palpable. Also, if you can palpate the spleen in a case in which you suspect a diagnosis of idiopathic thrombocytopenic purpura, it is highly advisable to consider some other diagnosis. My observations are based on 70 patients with various blood dyscrasias who underwent splenectomy within the last five years. In 60 per cent of the cases of idiopathic thrombocytopenic purpura, enlarged spleens were found—this despite the fact that in no case was the spleen palpable preoperatively.

In the other two hypersplenic syndromes, splenic neutropenia and splenic panhematopenia, the spleen is always palpable. If you cannot palpate the spleen, some other diagnosis should be considered.

Examination of the bone marrow is a prerequisite to the diagnosis of hypersplenism, and the first important factor concerning this examination is that it must be adequate. If a needle puncture of the sternal marrow is performed and an inadequate amount of tissue removed, either repeated needle aspirations must be done or an actual trephination of the sternum carried out so that enough tissue can be obtained for both fresh smears and block sections. In my opinion the removal of a spleen without an adequate bone marrow examination is inexcusable. I have seen 2 such patients, both of whom died. Undoubtedly the outcome would have been the same had splenectomy not been done, but they need not have been subjected to the operation.

A second point concerning bone marrow examination is the fact that in order to make a diagnosis of idiopathic thrombocytopenia one must find increased numbers of megakaryocytes in the bone marrow and they must be abnormal in that they present evidence of failure to discharge thrombocytes.

Third, in practically all hypersplenic states one must find evidence of myeloid and erythroid hyperplasia in the bone marrow before the diagnosis of hypersplenism can be made.

Fourth, and perhaps most important, the absence of hypoplasia must be established.

Normal bone marrow with a characteristic representation of the cellular elements and the lipoid content is shown in Figure 1. The

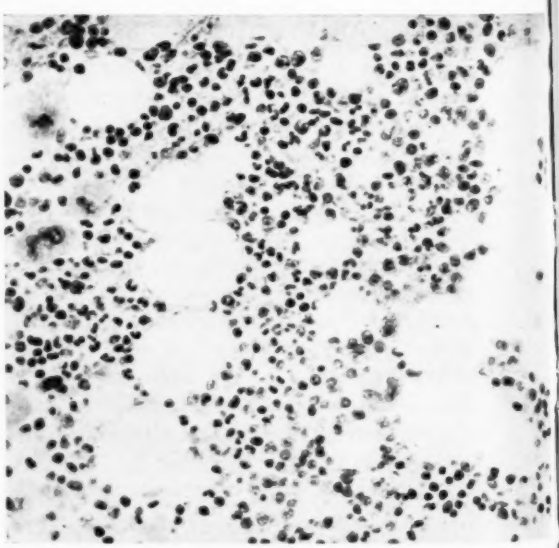


FIGURE 1. Normal bone marrow.

cellular elements are enormously increased in hyperplasia of the bone marrow, illustrated in Figure 2. This marrow is from a patient with congenital hemolytic icterus. Hypoplasia, the condition that warns the hematologist and the surgeon not to remove the spleen except for some prescribed experimental reason, is illustrated in Figure 3. No benefit can be obtained by removing the spleen in the presence of such a bone marrow.

In addition to establishing the absence of hypoplasia of the bone marrow, it is important to rule out other diseases for which

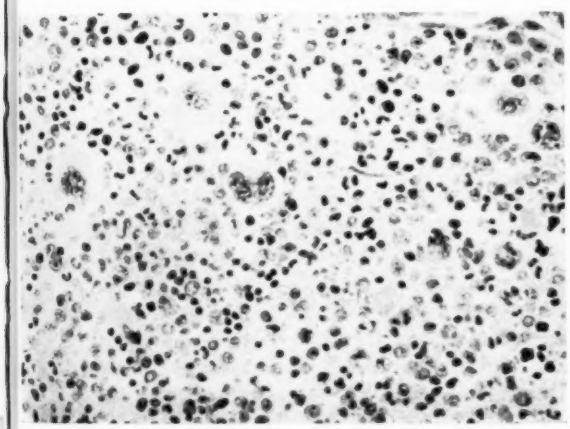


FIGURE 2. Hyperplastic bone marrow.

splenectomy is not necessarily indicated. Examination of the bone marrow permits the exclusion from consideration of such diseases as leukemia, lymphoblastoma, agnogenic myeloid metaplasia, thrombotic thrombocytopenic purpura, metastatic neoplasia, and others.

Hypersplenism is classified into one of two categories, primary or secondary. In primary hypersplenism the thrombocytes in the circulating blood are diminished in number, and this diminution must be observed on repeated examinations. When no other cause for this thrombocytopenia can be found, the condition is called idiopathic thrombocytopenic purpura. When the granulocytes are depressed the disease is termed primary splenic neu-

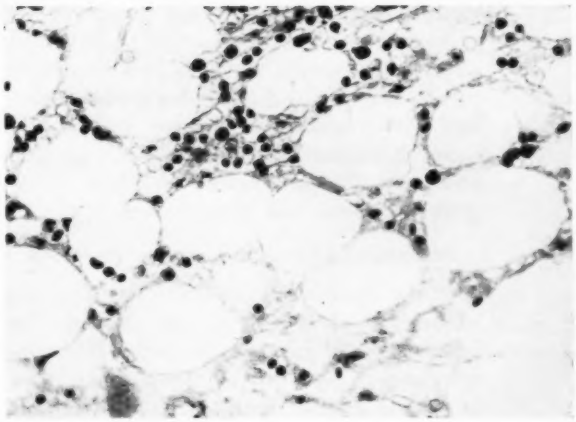


FIGURE 3. Hypoplastic bone marrow.

tropenia. When both thrombocytes and granulocytes are depressed the term panhematopenia, coined by Doan in 1944, or—perhaps a better term—pancytopenia, characterizes the syndrome.

In most instances of primary hypersplenism there is an associated anemia. The reasons for this anemia, not all of which can be demonstrated in each case, are (1) hemolysis, (2) blood loss and (3) interference by the spleen not only with the discharge of thrombocytes and granulocytes from the bone marrow but also with the development of the erythroid elements in the marrow.

Hemolysis—I do not consider hemolysis characteristic of the hypersplenic syndrome. Most patients who have pure thrombocytopenia or pure neutropenia or a combination of the two show no evidence of hemolysis. If occasionally hemolysis is the cause of the anemia in pure hypersplenism, the liver ordinarily is adequate to clear the blood stream of the increased amount of pigment produced.

Blood loss—Often it is difficult to ascertain blood loss in these patients, particularly in the gastrointestinal tract. Many of these patients lose blood into the subcutaneous tissues, oral cavity and genitourinary tract.

Interference with development of erythroid elements—This third cause of anemia is extremely difficult to prove, but many hematolo-

gists do feel that it is a distinct possibility.

Secondary hypersplenism is exactly the same disease except that it is associated with some other recognizable, diagnosable disorder. The commonly associated diseases are lymphoblastomas, leukemia, Boeck's sarcoid, Gaucher's disease, Felty's syndrome, and portal or splenic vein hypertension.

Idiopathic Thrombocytopenic Purpura

Of the more important syndromes that can be categorized as hypersplenic diseases, the first that I shall discuss is idiopathic thrombocytopenic purpura. Of all the purpuras seen in a large general hospital only 15 per cent are this type. The remainder may be caused by aplastic anemia, chemical agents, or ingestion or inhalation of toxic materials; they may have an allergic basis, or may be due to replacement of bone marrow by metastatic neoplasia or lymphoblastomas.

The question of allergy as a prominent factor in the pathogenesis of idiopathic thrombocytopenic purpura has been raised so often recently that one hematologist has stated that the diagnosis cannot be made unless there is definite evidence of an allergic etiology. Various factors substantiating an allergic basis are a family history and evidence of increased number of eosinophils circulating in the peripheral blood and in the bone marrow. In my experience only 20 per cent have an allergic background, and I do not believe that the presence or absence of allergy has anything to do with prognosis in idiopathic thrombocytopenic purpura, whether splenectomy is done or not.

It is not generally understood that idiopathic thrombocytopenic purpura in children is quite a different disease than it is in adults. I seldom advise or perform splenectomy for thrombocytopenia in children. In 90 per cent, there will be spontaneous remissions; a few will have minor recurrences but most ultimately will recover without permanent evidence of thrombocytopenia. Splenectomy for children with idiopathic thrombocytopenia is advised only if the acute episode goes on for several weeks, if bleeding is continuous or intermittent in such quantities as to endanger life, or if the child has repeated relapses.

In adults the story is quite different. Generally speaking, whenever the diagnosis of idiopathic thrombocytopenic purpura is made, no matter what the condition of the patient, I advise splenectomy.

The question of the preoperative transfusion of blood has been raised often. The primary reason for such transfusion is to elevate the number of circulating thrombocytes to assist in control of capillary bleeding. We have utilized such a procedure, using fresh blood given to the patient an hour or two prior to splenectomy, and I don't believe I can say it has assisted materially in the performance of the operation by controlling the capillary oozing from muscular tissue, serous membranes and skin. Nevertheless it does no harm and it may possibly do good.

Almost everyone who has encountered cases of thrombocytopenia has felt there is a relationship between thrombocytopenia and increased capillary fragility. Theories have been postulated that some vasoconstrictor substance is released by platelets or that platelets release something that interacts with a material in the plasma that produces vasoconstriction of terminal arterioles and assists in hemostasis in that fashion. Also, we all know that when platelets agglutinate they may form a plug that prevents bleeding from small capillaries and tiny arterioles. However, it has been my observation, and that of others, that many patients have a markedly prolonged bleeding time—20, 30 or even 40 minutes—prior to splenectomy and that following splenectomy there may be no rise in thrombocytes in the peripheral blood and yet in a few days the bleeding time has reverted to normal. It is difficult for me to associate the number of circulating thrombocytes in the peripheral blood with capillary fragility as measured by the bleeding time or by the extremity tourniquet test. The latter test, incidentally, is always positive in thrombocytopenia, in my experience.

How many of these patients can be cured by splenectomy? In our series 80 per cent had complete cures. Most of the others were benefited. In some there was no improvement. We

do not know the reason for the failures, but we do know that if by the fourth postoperative day the platelet count is not over 10,000, a remission that can be ascribed to the splenectomy is not apt to occur. It is true that some of these patients may have a normal circulating thrombocyte count after a period of many weeks or months, but it can hardly be called the result of the splenectomy.

Another observation I have made is that patients with bleeding times prolonged beyond 15 minutes are less apt to have a beneficial result from splenectomy than are those with bleeding times under 15 minutes.

Panhematopenia

The essential feature of panhematopenia is neutropenia, and the disease may be either acute or chronic. I have seen this syndrome develop in a period of four days to a point of complete prostration with no circulating granulocytes in the peripheral blood in a previously healthy individual. The symptoms are high fever, prostration, marked tachycardia and disorientation. The granulocytes disappear rapidly. The chronic form, which is most common, is manifested by subcutaneous ecchymoses, malaise, lassitude, symptoms of anemia, and oral or peripheral ulceration.

The epinephrine test has been used by some to suggest that the diminution of granulocytes in the peripheral blood is associated with sequestration of these elements in the spleen. That has not been my experience. The results of a characteristic epinephrine test are reproduced in Figure 4, and you will note the total rise following the administration of epinephrine was large but the greatest part of this rise was that in the number of circulating lymphocytes. Actually we have had patients in whom the polymorphonuclear leukocytes did not rise at all following this test. We also have had patients who had responses identical to this after the spleen was removed, so that we place very little reliance on the epinephrine test.

In cases of panhematopenia or pancytopenia, there may be an immediate response to splenectomy (Figure 5) as evidenced by an abrupt rise in the number of circulating granulocytes. In many other patients, however, the response is more gradual and occurs over a period of several weeks. If the diagnosis is correct, the response is always good. (Figure 6.)

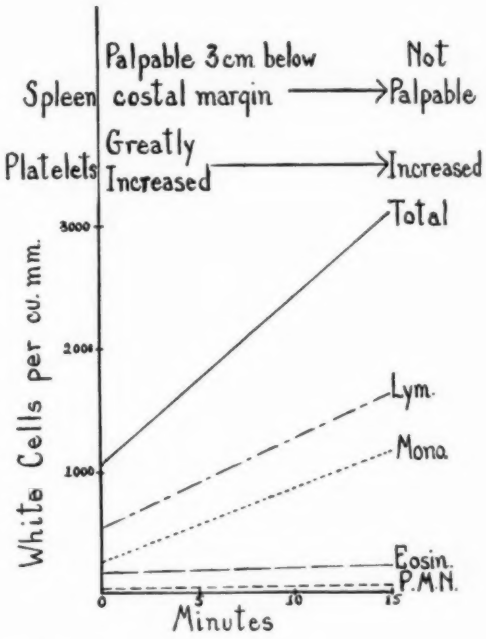
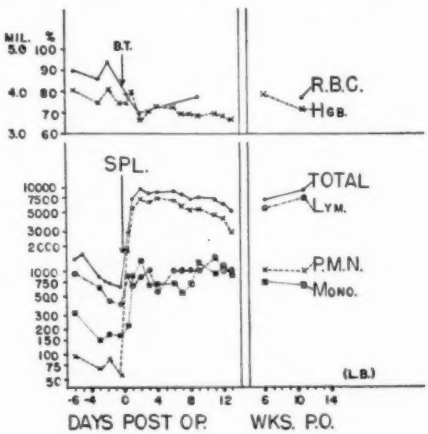


FIGURE 4. Epinephrine test.

FIGURE 5. Immediate response to splenectomy.



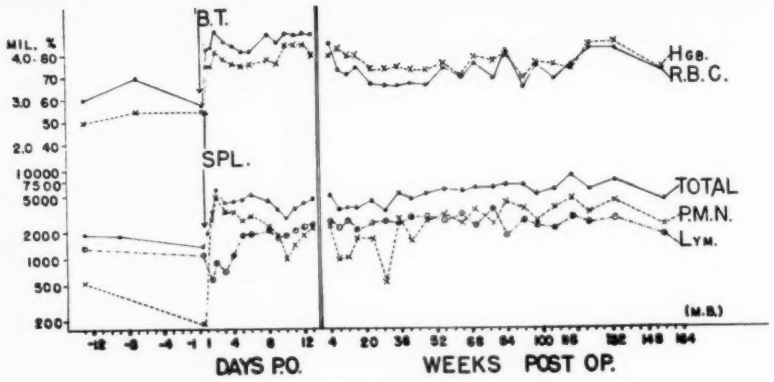


FIGURE 6. Response to splenectomy demonstrable over a period of several weeks.

Splenectomy for Splenism

As mentioned previously, splenism is a normal physiologic state. It has been proposed that by removing the normal spleen and thereby eliminating either the normal hemoclastic activity of the spleen or the normal inhibitory control of the spleen on the bone marrow, patients with congenital hypoplasia or even acquired hypoplasia of the bone marrow—persons who are not making their blood cells, either white or red, as rapidly as they should be—could be benefited. Dr. Dameshek has performed splenectomy in a certain number of these cases, and in 50 per cent he has noted beneficial results. We have performed splenectomy for this same type of patient in a few instances, and none of our patients has benefited whatsoever. What was hoped for, of course, was that in hypoplasia of the bone marrow, or aplasia, we could increase the interval between blood transfusions, but this result has not been obtained.

Why does splenectomy fail for the various hypersplenic syndromes? An accessory spleen left in the peritoneal cavity is one reason. Whenever splenectomy is done for thrombocytopenia, neutropenia, panhematopenia, congenital hemolytic icterus, acquired hemolytic disease—any one of the various diseases for which the operation is indicated—accessory spleens must be sought and removed. Occasionally they lie in very inaccessible and remote places such as under the splenic flexure of the colon. One patient on whom I operated actually had splenic tissue within the tail of the pancreas, and it was necessary to excise the tail of the pancreas in order to remove this tissue.

Another reason for failure is incorrect diagnosis. Still another is that the spleen is only one part of the reticuloendothelial system and that occasionally after splenectomy has been performed the other portions of the system, especially in the liver and the lymph nodes, take over the function that previously was carried out by the splenic sinusoids.

Cortisone and ACTH

We do not know as yet what effect cortisone and ACTH have on the hypersplenic syndrome. A few patients have been improved following administration of cortisone or ACTH either preoperatively or after the operation had failed. We cannot predict which patients are going to be benefited, and up to the present time we have seen no patients who were permanently benefited in whom we did not expect a spontaneous remission anyway.

A Breast Clinic

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Radical mastectomy for cancer of the breast has led to improvement in the 5 and 10 year survival rate. There is unlikely to be a further improvement because of the percentage of cases in which the growth has extended beyond the range of surgery. Super-radical operations have yet to prove their value. Pre- and postoperative radiations are worthy of trial in selected cases.

ROBERT M. JANES

THE patients who have come here through the courtesy of Dr. Stanley Hoerr of the Cleveland Clinic illustrate certain points in connection with management of tumors of the breast. The first patient, a 41 year old nulliparous woman, three weeks ago noticed a nodule in her right breast. There has been no discharge from the nipple, and no pain, and her menstrual history is normal. The nodule measures 1.5 cm. in diameter and is located in the medial and lower portions of the right breast. The skin is freely movable over it and there is no change in the nipple. There is no fixation to underlying fascia. When I attempt to obtain fluctuation I can detect elasticity in the lump. In other words, I think this is a single cyst of the breast.

I do not believe surgical exploration is necessary in all such cases. Many patients can be spared operation if a small needle—perhaps 20 gauge—is inserted into the nodule under local anesthesia to determine whether the mass contains fluid. If this is found to be the case, and if the contents can be aspirated completely and no blood is noted in the fluid, in my opinion no other treatment is required other than a follow-up examination six weeks or two months later. If no lump can be felt at the subsequent examination, nothing more need be done. It is, of course, essential that no questionable lump be left in the breast.

If the aspirated fluid contains blood, even if you suspect that it may be the result of touching the wall of the cyst with the aspirating needle, operation should be done. Blood in the aspirated fluid usually means papilloma or duct carcinoma projecting into the cyst.

I have utilized this method for about 20 years, and have kept very careful notes on the location of the original lesions. Occasionally such a patient is seen subsequently because of carcinoma or another cyst; I do not believe there is any important relationship between the two diseases, however, and when a cyst recurs you will find that the second nodule is almost always situated in another area of the breast.

The second patient, a 72 year old woman, came to the Cleveland City Hospital on November 3, 1952, because of a mass in the left

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breast of three months' duration. She stated that during that period the lump had doubled in size and there was dull aching pain around it. Examination discloses a firm, nontender mass 2 to 3 cm. in diameter in the upper and inner portions of the left breast, not fixed to the overlying skin or to the underlying fascia. There are no changes in the nipple or in the skin. No enlarged axillary or supraclavicular nodes are palpable. The right breast is almost normal on palpation, with perhaps some slight nodularity.

Diagnosis in this case presents a problem. The mass is rather smooth in outline and could again be a cyst. On the other hand, in a patient of this age one is inclined to be doubtful. Carcinomas in this age group are, in my experience, not infrequently of this particular physical character and often do not show skin attachment. So I would have no objection to the insertion of a fine needle into this mass just before preparing the patient for surgery, but I would suspect that this probably is a case of carcinoma.

This patient might be kept in mind when I discuss a philosophy of the management of carcinoma of the breast a little later on.

Not since the time of Halsted has there been so much soul searching, so much difference of opinion in regard to management of cancer of the breast. For many years it was accepted that radical mastectomy was a satisfactory operation and that it produced satisfactory results. Now there are those who on a purely statistical basis tell us that we have not in any way influenced the mortality rate from carcinoma of the breast in all these years.

While I do not subscribe to all the statements made by Park and Lees and by McKinnon of Toronto, their various articles do give one pause, and when one examines the over-all results of radical mastectomy one is rather chagrined to find that it is true that we probably have not increased by more than 10 per cent the five year survival rate. Statistics on patients who have been followed up without treatment disclose that 20 or 22 per cent of them survived five years, whereas slightly more than 30 per cent have survived that long after radical mastectomy.

In an effort to determine some of the reasons for this surprising finding, I would like to present some statistics, for which I am indebted to Dr. Delarue. Of all patients coming to see us, about 60 per cent have involvement of the axillary lymph nodes; of these, about 33 per cent also have involvement of supraclavicular lymph nodes and about 46 per cent, according to the studies of the younger Handley, have involvement of the lymph nodes along the internal mammary vessels. Of the 40 per cent who have no involvement of axillary lymph nodes, 11 per cent have involvement of the internal mammary chain. The incidence of mammary chain involvement in tumors of the inner quadrants of the breast is 60 per cent, and in tumors of the outer quadrants, 20 per cent.

In the face of such evidence it becomes obvious that we cannot solve the problem of carcinoma of the breast simply by radical mastectomy. However careful the resection may be, these patients have lymph nodes that are inaccessible.

Various approaches to the problem have been made. Some physicians carefully select the patients for radical mastectomy, omitting a certain group who are "categorically inoperable." By so doing, they have, of course, improved their statistics, but they also have discarded from consideration a large number of patients for whom they say nothing curative or of a worthwhile palliative nature is available.

Next there are those who advocate a superradical type of operation with removal of supraclavicular lymph nodes and/or parasternal nodes. Although the results of such drastic procedures still have to be determined, to me it is not conceivable that they are going to yield worthwhile dividends. Generally speaking I am not impressed with excessively radical operations for cancer, nor with their results. One has to take into account the morbidity and mortality rates and the long-term disability.

Another approach to the problem is the possibility of adding radiation in one form or another to surgery. This, of course, has been done in various centers for many years.

Finally there is hormone therapy, which undoubtedly has its place in the management of patients with advanced lesions. I will not discuss this form of therapy here, however, because I want to present a point of view and the results of the implementation of that point of view over a period of 10 to 12 years.

When I was associated with the late Dr. Gordon Richards while he was in charge of the Department of Radiotherapy at the Toronto General Hospital, we used preoperative radiation in treatment of some advanced cases of carcinoma. Our approach was somewhat different from that of others, in that the dose given was a cancericidal one and inevitably involved an amount of radiation which was about all that the skin would tolerate. We waited until the skin had returned to a state at which operation was possible—usually six weeks to two months—and then performed radical mastectomy.

The theoretical advantages of preoperative radiation are as follows: The radiation might destroy some cancer cells, particularly the rapidly growing ones; postradiation fibrosis might devitalize cancer cells and prevent local invasion by a wall of fibrous tissue; because of the sealing off with fibrosis, it might prevent the embolism of cancer cells, and perhaps it would be safer to divide the lymphatics that are full of cancer cells if those cells are devitalized and if their canal is partially or completely obstructed by fibrosis.

In order to analyze the results of preoperative radiation, one must know what type of radiation was given as well as what type of surgery was performed. We as surgeons are perhaps a little prone to forget that there is as much variation in the efficiency of radiotherapy as in the efficiency of surgery. Radiation therapy is a difficult and complicated procedure necessitating the employment of a well trained radiotherapist and a radiophysicist. One must know the size of the dose given, and the length of time between its administration and the subsequent operation.

In our series we quickly found that the ordinary classifications of the various stages of cancer of the breast were inadequate for our purpose. The ordinary Steinthal classification is now about 65 years old. We first utilized the Portmann classification, but found there was a considerable difference in behavior, depending on whether the case was stage 2 because of local conditions or whether it was so classified because of invasion of axillary lymph nodes. We then divided stage 2 into two subdivisions, and based our study on five stages.

The following listing shows the treatment employed for each of the stages:

Stage 1	Radical mastectomy only
Stage 2	Radical mastectomy plus postoperative radiation
Stage 3	Preoperative radiation and radical mastectomy (most frequently)
Stage 4	Preoperative radiation and radical mastectomy (all cases)
Stage 5	Radiation only; occasionally a simple mastectomy

We classify as stage 3 those cases in which there is attachment to fascia; there may or may not be actual invasion of the skin. Stage 4 is the advanced type of carcinoma, and stages 4 and 5 are subdivisions of the Steinthal stage 3. Stage 5 is that in which there are remote metastases, a condition that is obviously incurable by any method at present.

The biologic activity of the lesion must be considered. For example, a tumor of three months' duration and classified as stage 1 may be of a very different character from another in stage 1 that is of 12 months' duration. The latter tumor obviously is relatively inactive biologically.

In considering the results of preoperative and of postoperative radiation, I would like you to note particularly the cases in stage 4. It should be mentioned here that when it is stated that there is no clinical evidence of disease, this has been determined by roentgenographic study of the chest and of the skeleton, particularly the spine and pelvis. Following preoperative radiation in cases in stage 4, 41 per cent of the patients are alive at the end of five years, and 26 per cent have no clinical evidence of disease. In the same group, 15 per cent are alive after 10 years, and 13 per cent have no clinical evidence of disease.

As experience has increased, the results

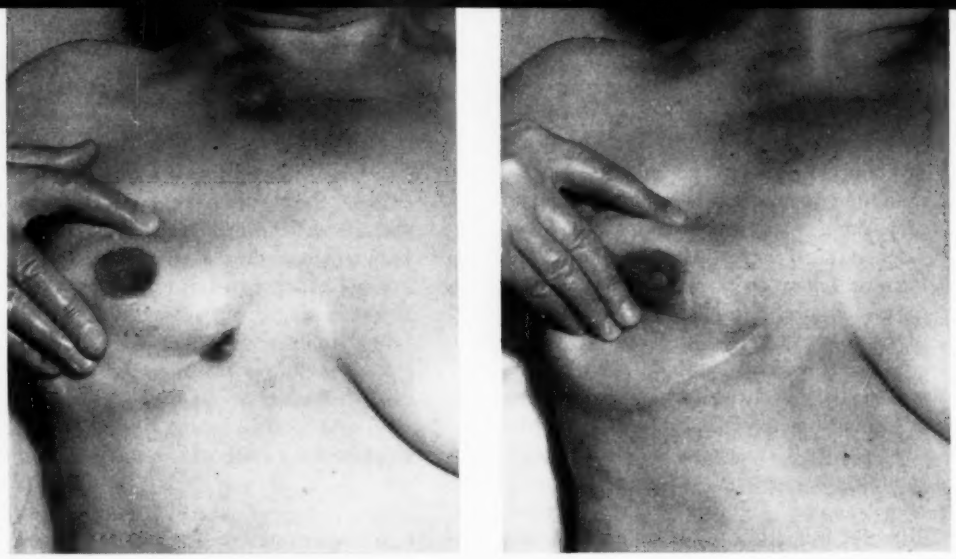


FIGURE 1*a*. November 18, 1937. Appearance of breast on admission. *b*. February 15, 1938. Condition three months following completion of preoperative therapy. *c*. April 12, 1938. Primary healing following radical mastectomy. There were no complications.

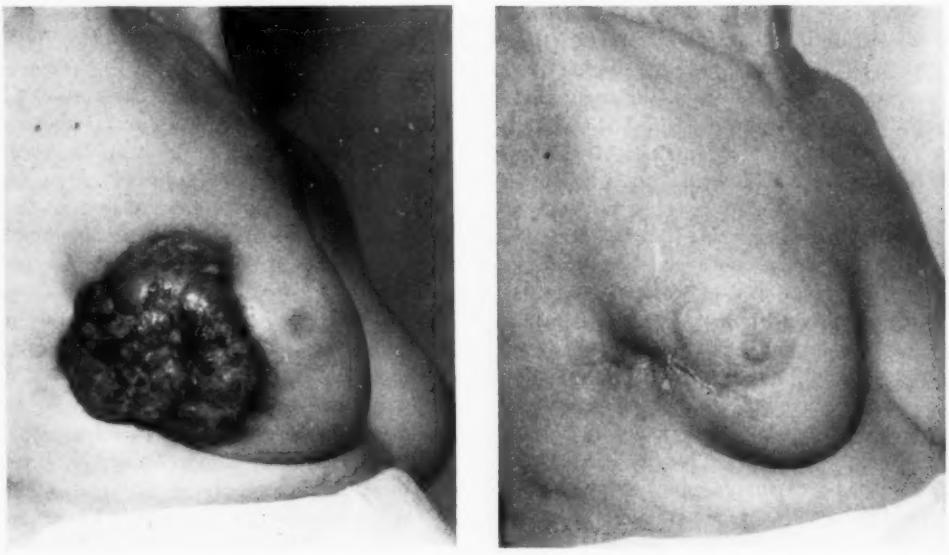


FIGURE 2*a*. February 1, 1938. Appearance on admission. *b*. September 20, 1938, seven months following completion of radiation. *c*. November 13, 1946. Condition of skin eight years later.

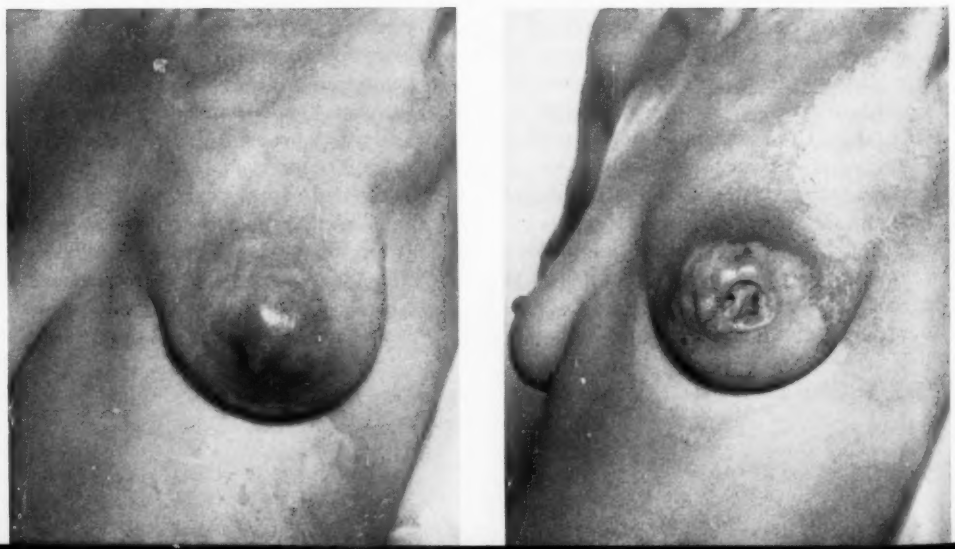
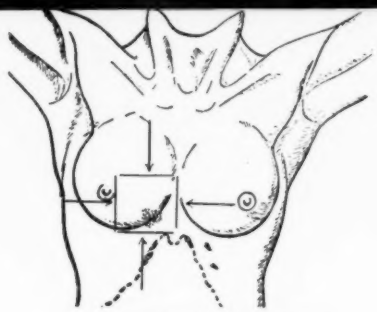


FIGURE 3*a*. April 12, 1938. Appearance on admission. *b*. July 5, 1938, immediately following completion of radiation series. *c*. November 13, 1946. Condition of skin eight years later.

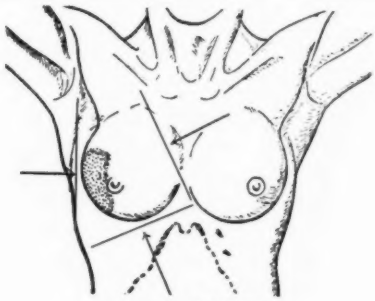


Breast—Teleradium Therapy
Tangential ports 8 cm.; T.S.D. 6 cm.

Superior		2000 r
Mesial		2000 r
Inferior		2000 r
Lateral		2000 r

Axilla—Teleradium Therapy

Direct		3500 r
Superior		5000 r
Right parasternal	200 K.V.	2600 r
Central epigastric	200 K.V.	2400 r



Breast—400 K.V.
Tangential ports—10 x 20 cm.

Superior-mesial	2900 r
Inferior-mesial	2900 r
Lateral-superior	2900 r

Axilla—Teleradium Therapy
Portal 6 cm.; T.S.D. 6 cm.

Direct, anterior and posterior	
Dose per port	4500 r

Supraclavicular—Two Ports

Teleradium therapy, dose per port	4500 r

Breast—400 K.V.
Tangential Ports—10 x 20 cm.

Superior-mesial	2000 r
Inferior-mesial	2000 r
Inferior-lateral	2000 r

Axilla—400 K.V.

Direct	10 x 15 cm.	Portal	1800 r

have improved. For example, for the first series reported on by Dr. Richards and myself, the five year survival rate was 32.5 per cent (40 patients), and 22.5 per cent had no clinical evidence of disease. For the most recent series, the survival rate is 50 per cent and the cure rate is 27.5 per cent. Sufficient time has not elapsed to obtain the 10 year results in this latter group.

Comparative statistics are always interesting. The five year survival rate for 22 untreated cases is 19 per cent. For a carefully selected series of cases at the Presbyterian Hospital, 50 per cent of the patients were alive after five years and 32 per cent after 10 years. In cases with involvement of the axillary nodes, the Presbyterian Hospital reports show a 20 per cent survival rate and the Memorial Hospital 21 per cent.

Bear in mind that in our series 88 per cent of those patients selected for preoperative radiation were classified in stages 4 and 5, cases in which ordinarily it would have been considered useless to undertake any definitive treatment. The five year survival rate is 40 per cent, and the 10 year survival rate is 16 per cent.

McWhirter's statistics show a 42 per cent five year survival rate for cases in which simple mastectomy was done, followed by postoperative radiation; the 10 year survival rate is 25 per cent, but 56 per cent of the patients were in the groups considered operable. We think that the 40 per cent five year survival rate in our patients who had advanced disease at time of operation is significant.

Figures 1 to 3 illustrate some representative cases in our series.

In conclusion, may I suggest that it is worth while, particularly in advanced cases of carcinoma of the breast, to consider the possibility of utilizing to the maximum what the radiotherapists can do for us. We believe that at present radiation is not important in stage 1 cases. If we can be sure they are properly classified and that operation is done properly, we do not advise radiation. Of course, stage 1 becomes stage 2 if pathologic examination discloses involvement of the axillary lymph nodes. In the latter instance we advise postoperative radiation.

In most cases in stage 3 and in all cases in stage 4, we advise preoperative radiation and radical mastectomy.

Operative difficulties are not greatly increased by use of preoperative radiation. Sharp dissection minimizes the problem, and healing is not greatly impeded if certain points are kept in mind. The skin has lost its elasticity; it has an adequate blood supply but will not stand tension. If tension is not produced, the skin will not slough much more frequently than in cases in which radiation was not employed. If the skin cannot be closed without tension, the area should be covered with a split skin graft.

We feel that a sufficient length of time has elapsed since institution of this method of treatment to indicate that it is yielding worth while dividends in these very difficult cases.

THE 1953 Assembly *OF THE*

INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

of North America

THE PALMER HOUSE, CHICAGO

November 2 to 5 (inclusive), 1953

Treatment of Pulmonary Tuberculosis

WINTHROP N. DAVEY*

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The problem of the control of tuberculous disease is far from being solved, even though great strides have been made in the use of antituberculous agents and the addition of refinements in surgical technics, particularly those of pulmonary resection. The more urgent problem, however, is that of establishing the diagnosis of pulmonary tuberculosis early. Only in this way can tuberculous persons be isolated and the spread of tuberculous disease precluded.

WINTHROP N. DAVEY

TUBERCULOUS disease, accounting for more deaths annually than any other cause, continues to present the most challenging medical problem in the world today. In the United States tuberculosis is still the most common cause of death between the ages of 15 and 35 years; yet paradoxically it is becoming a disease of older persons, particularly men in the sixth and seventh decades of life. This assumes even greater importance when one realizes that the incidence of other pulmonary diseases, particularly bronchogenic neoplasms, also is increasing in these same age groups.

In the United States, those of us engaged in the care and treatment of patients with tuberculosis have much to be thankful for. The decrease in infectivity, morbidity and mortality rates has been very gratifying. Since 1900 the mortality rates from tuberculous disease have decreased from approximately 200 per 100,000 persons to less than 20 per 100,000. This lowered mortality rate, though most gratifying, unfortunately does not represent the true picture of tuberculous disease.

The infectivity rate continues to be in excess of 50 per cent, as demonstrated by tuberculin skin reactions. The morbidity rate varies from 0.1 to 0.3 per cent, as shown by chest x-ray surveys, and the continuing mortality rate is about 0.0002 per cent. This means there are more than 75,000,000 individuals in the United States who are infected with viable, pathogenic tubercle bacilli which are patiently awaiting an opportunity when the general resistance of the hosts is so lowered through malnutrition, intercurrent illness or other stress that they can manifest their well known characteristics of opportunism.

Some 400,000 Americans have active, open pulmonary tuberculosis. These individuals are releasing tubercle bacilli intermittently or continuously into their immediate environment and constitute a great hazard not only to themselves but also to their associates. Unfortunately, fewer than one-half of these 400,000 persons are known to our public health agencies, and only slightly more than one-half of those with recognized tuberculous disease are now hospitalized, for there are only about 125,000 beds available for these patients.

These hospitalized patients account for the majority of the 30,000 annual deaths and are the specific problem of physicians engaged in

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the care and treatment of tuberculous individuals in our sanatoriums.

More important, however, to the general practitioner is the care of the general population in the communities, which includes the 75,000,000 cases of potential reinfection tuberculosis, the 200,000 cases of active, open tuberculosis and the unknown number of potential cases of first infection tuberculosis—individuals who now react negatively to tuberculin but who may at any time acquire tuberculous disease from persons with new or long-standing open cases.

In more than 50 per cent of these new cases, the patients admitted to sanatoriums have advanced pulmonary tuberculosis, hardly amenable to the routine forms of therapy. Thirty-five per cent have moderately advanced tuberculosis, necessitating rather prolonged hospitalization and often surgical intervention. Fewer than 15 per cent have minimal pulmonary tuberculosis which in extent and usually in duration is most amenable to current forms of therapy.

Methods for early detection of tuberculous disease have long been available. Through skin testing, serial chest x-rays and careful sputum evaluations, including gastric concentrates, cultures and guinea pig inoculation, the majority of cases can be diagnosed in their incipient and usually minimal stages. The use of serial chest x-rays and the follow-up of those individuals who show evidence of pulmonary disease is our only hope for diagnosing tuberculous disease in a minimal and early state. Such surveys should be repeated at intervals of one year, and even at this interval only 70 per cent of the persons found to have tuberculosis will have minimal disease, the remainder having more advanced disease and some 15 per cent showing evidence of cavitation.

Dr. Stocklen from Sunny Acres Sanatorium in Cuyahoga County (Ohio) has been most kind in sending 2 of his patients, and I would like to describe them to you.

The first patient is a 19 year old college student from Ohio State University. In March 1952, while a sophomore, she had a tuberculin skin test which was positive. She had not had a prior tuberculin test to her knowledge, but because the test was positive she had a chest x-ray taken at the university. She had had previous chest x-rays by a mobile unit in the Cleveland area, but she had not heard from those physicians concerned with the films and had assumed they were negative.

The chest x-ray taken at college showed evidence of minimal disease in her left upper lung field, and it was suggested that she return to her home in Cleveland and visit the county clinic. She had additional chest x-rays and was started on streptomycin and para-aminosalicylic acid as an outpatient. Since then she has received 1 gm. of streptomycin twice weekly and 12 gm. sodium PAS orally daily.

She had to wait until June 30 before she could be admitted to the sanatorium, and she had a therapeutic pneumoperitoneum on July 15. She has been continued with combined intermittent streptomycin and continuous PAS therapy since the time of the diagnosis of her minimal pulmonary tuberculosis.

There has been no bacteriologic confirmation of this patient's disease, repeated gastric concentrates and cultures having been negative for tubercle bacilli. The bacteriologic confirmation of tuberculous disease, though helpful, is unnecessary in cases of minimal involvement. This patient is now ambulatory.

The second patient is a 44 year old man, a construction worker, who in 1944 at the time of examination for Army induction was found to have disease in his right upper lung field which was considered tuberculous. He underwent sanatorial care at Sunny Acres, and has had a temporary interruption of the right phrenic nerve and therapeutic pneumoperitoneum. He remained at the sanatorium for 10½ months, and during this time was slowly returned to activity.

He had bacteriologic confirmation of his disease. With continued paralysis of his right hemidiaphragm it was unnecessary to repeat the phrenic crush, and pneumoperitoneum was continued with satisfactory elevation of the right hemidiaphragm.

A roentgenogram taken in May 1944 shows a soft-appearing area of disease in the right upper lung field with areas of relative rarefac-

tion at the first anterior rib and first anterior interspace and some elevation of the diaphragm on the right; the temporary phrenic nerve interruption was performed prior to the induction of pneumoperitoneum.

A subsequent film taken four years later shows evidence of continued improvement in the right upper lung field, with marked elevation of the right hemidiaphragm and air in the peritoneal cavity.

The pneumoperitoneum therapy was continued for six years and the patient returned to work during most of that time.

In 1950 the pneumoperitoneum was abandoned but he returned to the clinic periodically for chest x-rays. An x-ray taken in March 1952 shows evidence of residual disease in his right upper lung field, which is undoubtedly caseous; there is continued elevation of his right hemidiaphragm, and the fluoroscopic evaluation of its function is unknown. Later, in August 1952, there was x-ray evidence of increase in the disease in his right upper lung and he again had positive sputum.

He was readmitted to the sanatorium in September 1952 and began a course of streptomycin and PAS on an outpatient basis, and this is being continued at present.

He tells me that it has been contemplated that he will need surgical resection of the residual disease in the right upper lung field after a preparatory course of antibiotics.

Sanatorial care, including general bodily rest, continues to be the basic form of management of tuberculous disease and particularly of pulmonary tuberculosis. This form of bodily rest may be a modified form of bed rest and not strict confinement to bed, this varying with geographic location of the sanatorium and training of the physicians.

The almost spectacular advances which have been made in the control and treatment of tuberculous disease since the advent of the antibiotics and the refinement in surgical technics, particularly those of pulmonary resection, have been very useful in the care of tuberculous patients.

The antimicrobial agents which are effective against *Mycobacterium tuberculosis* are few. Those in which particular interest has been shown include the sulfones, of which PROMIZOLE®, DIASONE® and PROMIN® are examples; the thiosemicarbasones, of which tibione, or TB 1-698, is the most widely known; the amino-hydroxybenzoic acids, of which para-aminosalicylic acid is the best known example; the antibiotics, including penicillin, streptomycin, chloramphenicol, neomycin, AUREOMYCIN®, terramycin and viomycin; and the recently considered pyridine carboxylic acid, or isonicotinic acid derivatives, of which isoniazid, or isonicotinic acid hydrazide, and iproniazid, or its isopropyl derivative, have been of increasing interest.

Unfortunately the majority of these antimicrobial agents, with the exception of promizole, streptomycin, PAS, viomycin and the recently employed isonicotinic acid derivatives, have proved to be either too toxic when employed over long periods of time, as is necessary in the treatment of tuberculous disease, or ineffective when employed in vivo. Also, it has been shown that they become ineffective because of the rapid emergence of strains of tubercle bacilli which are resistant to the agent.

The use of promizole is limited because it is relatively weak in its antituberculous activity and is somewhat toxic when used for prolonged periods of time. Neomycin is quite toxic when employed parenterally.

Terramycin, penicillin, chloramphenicol and aureomycin are essentially ineffective in the treatment of tuberculous disease.

Tibione, or TB 1-698, is extensively employed in Continental Europe, probably due to the paucity of available streptomycin, but is quite toxic to the liver, kidneys and hematopoietic system.

This leaves streptomycin, PAS, viomycin and the isonicotinic acid derivatives as satisfactory antimicrobial agents in the control of tuberculous disease.

The accepted antimicrobial therapy of tuberculous disease at present is prolonged combined intermittent streptomycin and continuous PAS therapy. The streptomycin is given in a dosage of 1 gm. in a single injection either two or three times weekly, and the PAS in the form of a sodium salt orally daily

to an equivalent of 12 gm. of the acid salt. The latter is given in four divided doses with meals and a bedtime feeding because of gastric irritation and intolerance which develop in most persons if it is not given with food.

Duration of therapy depends entirely on the clinical situation. It is generally agreed that a minimum of four months is indicated. The majority of phthisiologists continue treatment for not less than eight months, and some as long as 18 months to two years.

The results of this program of therapy have been most dramatic. Needless to say, those areas of disease which are primarily exudative and apparently more readily reversible show the most striking evidence of improvement under such therapy. That there still remain areas of residual disease, sometimes cavitary and almost always necrotic, makes it even more necessary that there be a close physician-surgeon relationship early in the patient's treatment.

It has been shown conclusively by Medlar and others that these residual areas of disease in the lung, even after prolonged periods of antibiotic therapy, contain numerous tubercle bacilli. In the majority of instances these tubercle bacilli are incapable of growing in cultural mediums and will not produce progressive tuberculous disease in the guinea pig, but there is no proof that these organisms are truly dead and will never again be capable of producing disease. Because of this lack of evidence, there has been a definite trend toward surgical extirpation of these residual necrotic lesions and this trend is continuing.

The object of such surgical extirpation is to remove the smallest volume of nonfunctioning lung tissue possible with the resection of the necrotic disease. Though pneumonectomies and lobectomies will continue to be very important, it is hoped that the majority of such procedures can be limited to segmentectomies, wedge resections, block resections and enucleations.

Those patients who seem likely candidates for such a program (and I wish to stress that there is no agreement on the criteria for this determination) are at present not likely to receive the conventional forms of reversible collapse therapy, including pneumothorax, pneumoperitoneum and temporary phrenic nerve interruption. I repeat, this is not uniformly accepted, and certainly pneumoperitoneum with or without combined temporary phrenic nerve interruption continues to be a very popular form of reversible collapse therapy which is apparently very useful but is perhaps not necessary.

It is obvious that many patients with tuberculosis will not be candidates for such therapy, if only because of the extensive destruction of lung. These persons either will not survive or will be candidates for the already conventional forms of reversible and irreversible or permanent collapse therapy that have been so useful in the past.

That the derivatives of isonicotinic acid when added to our present armamentarium of antimicrobial control of tuberculous disease will give even better results is our fondest hope. These drugs, isoniazid and iproniazid, are already very promising even when employed alone, and when employed in conjunction with other chemotherapeutics this promise may be fulfilled.

We often say jokingly that either tuberculosis will now be controlled entirely by the use of tuberculostatic drugs, if the tubercle bacilli which remain in these necrotic foci are truly dead, and that surgical removal of such disease will not be necessary, or tuberculostatic drugs will be employed only as preparatory therapy for the surgical removal of practically all the residual disease in the lung. Of course the true situation undoubtedly will lie somewhere between these two extremes. It will be possible to clarify more carefully the indications for such surgical resection, and to determine which individuals will be likely candidates for the reception of this therapy, and there will be continued progress along these lines with the use of tuberculostatic agents for prolonged periods of time until it is possible by the use of tuberculostatic or tuberculocidal agents to render patients with tuberculous disease truly free of viable tubercle bacilli. Even then it may be necessary to remove the residual lesions, particularly if cavitary.

Radioactive Iodine in the Medical and Surgical Management of Goiter

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The role of radioactive iodine in the management of thyroid enlargements is discussed aside from the ordinary problems of assessment of total thyroid function. Radioactive iodine is of definite value in the differential diagnosis of thyroid nodules. Therapeutically, radioactive iodine is especially valuable in hyperthyroidism.

MORRIS T. FRIEDELL

WHEN radioactive iodine is given either orally or by another route, it acts just as ordinary iodine would. It is taken up by the thyroid; it is excreted by the kidney; it finds its way into other body tissues in very minute amounts, and the rate of its uptake in the thyroid gland depends entirely on the activity of that gland. The mechanism is known as an iodide trap, and apparently any type of iodine —inorganic or ionized form, a suspension in oil, a combination of iodine with renal, excretory or gallbladder dye—will find its way to the thyroid gland, and act as a reservoir and continue to affect the gland for some time. This mechanism, therefore, will interfere with the use of radioactive iodine in the study and treatment of thyroid conditions.

After the iodine has passed through the cells, which apparently takes a very short time and depends again on the activity of the cells, it is stored in the colloid in organic form as thyroglobulin and converted into the hormone thyroxin, which is secreted into the blood stream. The latter mechanism apparently has to do with the states which we consider clinically as hyperthyroidism and which are really reflections of hypermetabolism, because it can be demonstrated that radioactive iodine occasionally is taken up and stored in the thyroid gland in rather considerable quantities in the absence of any clinically apparent alteration in the patient's condition.

Ordinarily, if the thyroid gland is hyperactive, 50 to 100 per cent of a dose of radioactive iodine will lodge within the gland in the first 24 hours which follow administration. For average clinical work it is necessary only to apply a Geiger counter to the thyroid gland at a constant distance with previously calibrated measurements—which are not too complex, although the instrumentation, of course, is—and measure the amount of iodine which lodges in the thyroid gland during a 24 hour period. The minimum amount in a normal thyroid gland varies in different laboratories, depending on the standards which have been set up. In our laboratory we consider 15 to 35 per cent as being within normal limits, and ranges somewhat below and above that as indicating borderline states of either underactivity or overactivity.

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After a small tracer dose of radioactive iodine has been administered and the activity of the thyroid gland estimated, it becomes possible to decide not only what should and can be done for the patient but also what might be within that thyroid gland that may or may not be palpable externally.

The effect of the radioactivity resulting from larger doses of radioactive iodine—as the physicist says, in millicurie doses—0.15 millicurie per gram of thyroid tissue, is ordinarily enough to destroy the gland structure providing the iodine is retained. It is not enough for this radioactive material to pass through the thyroid gland; it must stay there, and a good bit of it must undergo physical decay in order for it to have any effect. In addition to affecting the thyroid gland it also affects the blood supply to the gland.

Use of radioactive iodine is accepted therapy in certain hyperthyroid states, in older persons and in patients who present definite surgical risks because of associated clinical conditions such as cardiovascular disease, diabetes, tuberculosis or rheumatic heart disease. It is quite effective in progressive severe exophthalmos; in our experience, at least, there has been no exacerbation of exophthalmos in several hundred cases in which the patients were treated with radioactive iodine. Not all cases have shown regression, it is true; about 80 per cent have regressed and the remaining 20 per cent have remained stationary or perhaps improved slightly. It should be noted that as the patient gains weight the exophthalmos is less noticeable.

Radioactive iodine is also indicated for patients who are refractory to propyl thiouracil and ordinary forms of medical management, including use of Lugol's solution. It is especially useful in cases of recurrent postoperative hyperthyroidism.

A 47 year old woman who was refractory to propyl thiouracil and thus could never be prepared for surgery presented a diffusely enlarged hyperplastic thyroid with onset of exophthalmos (Figure 1a). She was given a tracer dose of radioactive iodine, which indicated that her thyroid gland was overactive—approximately 85 per cent of the dose was taken up by the gland in 24 hours. After calculation of the uptake plus estimation of the size of the gland (it probably is always larger than we think), a therapeutic dose was admin-

FIGURE 1a *(left)*. Woman 47 years of age with hyperthyroidism. b *(right)*. Same patient three months later, after treatment with a single therapeutic dose of I^{131}.

FIGURE 2a *(top)*. Carcinoma of the thyroid gland in a patient with hyperthyroidism. b *(bottom)*. Same patient three months after administration of huge dose (100 millicuries) of I^{131}. The hyperthyroidism disappeared but the nonfunctioning carcinoma was not affected.

istered so that approximately 0.15 millicurie or 150 microcuries of radioactive iodine would be retained within the gland per gram of thyroid. That is the only treatment this patient had. Within two weeks the size of the gland began to decrease, and three months later the thyroid enlargement had disappeared completely (Figure 1b). She began to gain weight and her exophthalmos regressed quite promptly. Clinical improvement takes a little longer than is the case with ordinary therapy, including Lugol's solution, but after the second week the response is good.

In some cases there will be a slight exacerbation of hyperthyroidism during the first week following therapy with radioactive iodine, and if these patients are acutely ill it is wise to administer Lugol's solution in small amounts for five to seven days, beginning on the third or fourth day after the therapeutic dose of radioactive iodine.

Hyperthyroidism sometimes occurs in association with other disease states. One patient with an uptake of radioactive iodine of almost 100 per cent had a massive enlargement of the neck on one side which was due to a tumor of the thyroid gland (Figure 2a). The radioactive iodine was well distributed over the normally located area of the thyroid gland, but there was no evidence of radioactivity over the tumor mass. A biopsy was done. Huge therapeutic doses (100 millicuries) of radioactive iodine were administered. Roentgen ray therapy was instituted. The lesion, which obviously was inoperable, promptly broke down and fungated (Figure 2b) and the patient subsequently died.

Some contraindications to the use of radioactive iodine should be mentioned. We are somewhat afraid to subject adolescent patients to this form of treatment when other

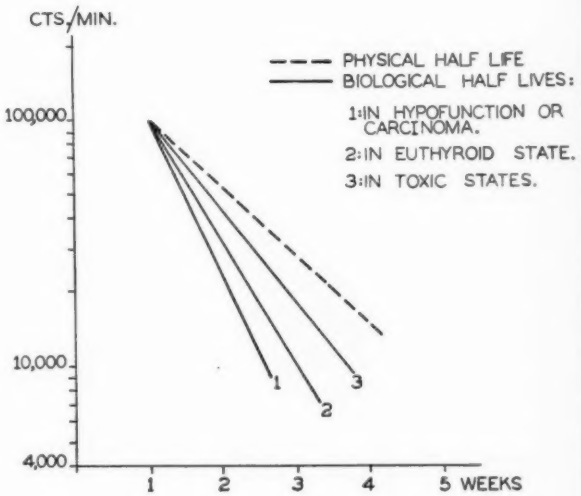

FIGURE 3. Comparison of rate of disappearance of I^{131} from the thyroid gland in various conditions.

methods are available which will carry a relatively minor amount of risk—premedication with the thiouracils and Lugol's solution, and surgery.

Radioactive iodine is contraindicated during the late months of pregnancy. The fetus develops its thyroid after about the fourteenth week, and one does not want to irradiate the thyroid gland of the fetus.

Figure 3 illustrates what happens to radioactive iodine after it has lodged in the thyroid gland. From week to week there is a definite disappearance of the radioactivity in the thyroid gland, apparently related to the activity of the thyroid itself. The dotted line, the true physical half-life, indicates how much would disappear—50 per cent. The solid line numbered 1 represents the biologic half-life in carcinoma, and demonstrates that while the carcinoma may pick up radioactivity, it will not retain it for as long a time as will the normal thyroid gland (solid line 2) or the thyroid gland in hypothyroid or hyperfunctioning states (solid line 3).

In a series of 160 cases of thyroid enlargement there were 2 instances of carcinoma in 100 patients who were toxic. Both these patients were women. Of 60 nontoxic cases, 6 were of carcinoma, an incidence of 10 per cent compared with an incidence of 2 per cent in cases of hyperfunctioning thyroid. This indicates that the radioactive iodine assessment of thyroid function will at least suggest the type of abnormality within the thyroid gland.

We have broken down these series of cases into the various types of palpable enlargement plus the findings at surgery. There were 46 patients with diffuse enlargement, 1 of whom had cancer; of 14 cases of unilateral enlargement, 1 patient had cancer; 23 patients had single toxic nodules, none of which proved to be malignant, and 15 patients with toxic thyroids presented diffuse multiple enlargements. Of the latter, no case has been proved to be carcinoma, at least up to the present.

Of the cases of nontoxic enlargement, 31 were diffuse, and the incidence of carcinoma was 6.4 per cent, whereas if one combines the cases of unilateral enlargement and of solitary nodules, one finds that there were twice as many carcinomas in that small group, an incidence of almost 14 per cent. This finding coincides with our previous reports that a nonfunctioning unilateral or single nodule of the thyroid gland has an incidence of carcinoma of 10 to 25 per cent.

Three patients whom I shall describe demonstrate some of the findings. Bear in mind that the constants will not be accurate, but we do have enough evidence to indicate some of the things that can be done in the laboratory.

The first patient, an 18 year old man, first noticed some nervousness, loss of weight and rapid pulse rate a year and a half ago. Questioning brought out the statement by the patient that his neck had always been somewhat enlarged, but he paid little attention to it until the symptoms developed. He was managed on propyl thiouracil and Lugol's solution for about a year, when treatment was stopped. About three months ago there was a return of symptoms, but they were not severe enough to trouble the patient until about a month ago. Now what shall we do with this lad? Two methods of treatment are available: surgery and radioactive iodine. He has been given a tracer dose of radioactive iodine, and Dr. Roberts will demonstrate the radioactivity present within the thyroid gland. Every click of the Geiger counter represents a considerable amount of radioactivity passing through the register, and if we compared this percentage of counting rate with the previously administered dose we could determine quite accurately the amount of overactivity in this thyroid gland. He has a rather diffusely enlarged thyroid, weighing, I would imagine, about 75 gm.—and if my estimate is 75 gm., it probably weighs 90 or 100 gm.

There is little difference in the amount of radioactivity between the two sides of the thyroid gland, which would tend to confirm our opinion that this is a diffusely hyperplastic gland. Occasionally, after long-continued administration of propyl thiouracil, nodular areas develop, but these are not apparent in this case.

The only objection to giving this boy radioactive iodine is a theoretical one; we do not want to subject him to radioactivity without

knowing what its long-term effects will be in 20 or 30 years. So far, no untoward effects have been reported following use of this material, and some of the patients were treated 10 or 12 years ago. However, the objection is still present, and the younger the patient the less anxious I am to use radioactive iodine.

What if this boy does not respond to propyl thiouracil and Lugol's solution; in other words, what if he cannot be prepared safely for surgery? Then I think radioactive iodine should be used. There is no question that the gland will regress and the symptoms will disappear, and the chances of hypothyroidism developing when the doses are accurately calibrated are 2 to 4 per cent. Neither is there any question of recurring nerve paralysis or any other hazards which accompany ordinary thyroidectomy, and the incidence of hypothyroidism is approximately half of what it is in radical thyroid surgery.

The next patient presents a somewhat different problem, namely, what can be learned about the thyroid gland with a tracer study. This 70 year old woman has a nodular thyroid. In addition, she has diabetes and has had a radical mastectomy. Obviously she is not a surgical risk, and she is the type of patient in whom we would like to know the exact status of the thyroid gland before we consider thyroidectomy.

When we place the Geiger counter over her neck, various areas of hyperactivity and of hypoactivity are evident, but the total uptake is 40 per cent or less, no matter how one calculates it, indicating that hyperthyroidism is not a pressing problem. There is prominent enlargement of the thyroid on the right side, but the enlarged nodule functions quite satisfactorily.

It has been our experience that a hyperfunctioning nodule is never malignant. That sounds like a very definite statement but actually it is true. We have found, at least up to the present, that carcinoma of the thyroid gland almost never takes up more radioactive iodine than the normal thyroid areas, and almost always takes up less. Thus we can say that this particular nodule is probably not malignant. This finding is helpful, because we are not anxious to operate anyway, because of the associated conditions which will interfere with a good surgical recovery.

The third patient presents a unilateral thyroid enlargement. His thyroid gland is about three to four times the size of that which you would expect to find in a man of his age. This enlargement has been present for many years. There have been no symptoms, and I am sure that someone has told him in the past, "If it doesn't bother you, don't bother it," which is really not a wise thing to say to anyone who has a lump any place. Dr. Roberts is holding the Geiger counter over his thyroid gland, and we can tell exactly, by means of a clock, what the counting rate is. The amount of radioactivity over the thyroid enlargement is definitely decreased. We have refined this technic by shielding the counter with lead so that no other radiations can sneak in, and making the aperture very small. In this way we can actually scan the entire thyroid area and pick out all the areas of function. Being clinicians, of course, we don't suspect the thyroid gland until we can feel it, and when we palpate a nodule we are curious about it. The nodule in this case has enlarged during the past year, and function within the nodule is not as high as in the remainder of the thyroid gland.

What causes that? That becomes the problem. Obviously one of the ways to find out is to take a biopsy specimen or, better yet, to remove the entire lobe. However, we have a basis on which to urge this man (who is in his sixties) that the latter probably is the wiser procedure. If there were no function in this nodule—no radioactivity whatever—only a few conditions would have to be considered: Fetal adenomas do not take up any form of iodine; a thyroid cyst which contains no functioning thyroid tissue will, of course, not take up radioactive iodine, nor will a degenerated calcified nodule. The latter two conditions can be diagnosed rather easily; a cyst is palpable and so is an extremely hard nodule. The only other lesion which will not take up radioactive iodine is a rapidly growing carcinoma, an undifferentiated carcinoma which does not function. Obviously that is not present in this case, at least at the present time, since the nodule

does function. The diagnosis probably lies somewhere between a colloid nodule, an embryoma which may or may not be a premalignant lesion, or a papillary adenocarcinoma or low grade undifferentiated adenocarcinoma. In other words, here is a tumor which is not functioning quite as much as normal thyroid tissue, but nevertheless takes up some radioactive iodine, and we now have a basis on which to say to this man, "This is what is happening in this particular nodule. You do not have hyperthyroidism. We do not have to worry about a surgical risk. The operation actually is almost minor in character because there are no associated complicating factors which would increase the risk."

Suppose, for example, we found this mass had a total uptake in the neighborhood of 75 per cent—a toxic thyroid with a nonfunctioning mass. The problem would be the same, but an added problem would be that of the patient's preparation. I would like to point out that he can be prepared by ordinary means. When a person has goiter and gets propyl thiouracil there usually is an enlargement and an exacerbation, so he probably is better off if he is given iodine instead. Or he can be prepared for surgery if we give him a dose of radioactive iodine and wait a month; in this way the operation should be done without any particular difficulty.

From the standpoint of diagnosis, therefore, we are able to map out the entire thyroid function, to find out whether hyperthyroidism is present and, in addition, to determine the amount of activity present in each of these thyroid enlargements and predict, at least to some extent, what their status is.

Postgraduate Clinical NOTES

7. HYDROCORTISONE ACETATE

Hydrocortisone acetate, injected 7,352 times into joint spaces, bursae, and tendon sheaths in the treatment of various localized rheumatic conditions, has been successful in at least partially ameliorating inflammation for extended periods in about 85 per cent of the 723 cases studied. It is still too early, however, to suggest that this method be accepted as a standard adjunct for local management of rheumatic conditions. Two years of observation leave us still optimistic, but only time will tell whether this alleviating effect will result in the long-term benefit the physician seeks for his patient.

The dangers from this type of therapy thus far appear minimal, providing proper diagnostic studies have been made and technic is carefully followed. The limitations of intra-articular treatment are fairly obvious. So far, the main contraindication to such treatment has been the presence of infection in or near the joint.

This therapy is useful alone in localized disorders. In systemic diseases, it should be combined with accepted general treatment.

Hollander, J. L.: Local Therapy of Arthritis and Related Conditions. *The Merck Report*, April 1953, page 8.

The Present Status of the Treatment of Gastric Malignancy

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Successful treatment of gastric cancer is related to early recognition of these tumors and dependent on more thorough surgical removal of all cancer tissue. In many cases this will mean a total gastrectomy. Radical surgery is indicated when more thorough removal of all cancer tissue is thus insured and when such extensive operations can be done without increased morbidity or increased mortality. Operative mortality with total gastrectomy is approximately that of partial gastrectomy. If our five year survival rate can be increased and the operative mortality not be increased, a more extensive operative procedure such as total gastrectomy is justified.

SAMUEL F. MARSHALL

THE treatment of carcinoma of the stomach is still a considerable problem, probably because of a great air of pessimism that seems to surround the matter of treatment. I doubt whether this is altogether justified, because some patients—a small group, of course—are still alive and well more than five years after resection. I think it is important to overcome this spirit of pessimism and to bring to you some of the features concerning the recognition of carcinoma of the stomach and its treatment in order to improve, perhaps, the lowest survival rate of any type of cancer in the human body.

Treatment depends fundamentally on two factors: (1) the most important, early recognition and (2) the methods of surgical treatment available. In the light of our present knowledge, surgical extirpation of the tumor is the only method that we have for treatment. It may be possible in the future that some form of higher volt radiation therapy obtained by the two million volt machines will help us to a great extent, but so far this type of radiation therapy has been used only as a palliative measure.

The problem that presents itself is, I think, simply this: What can we do to improve the screening methods in determining the diagnosis of early carcinoma? Screening methods based on the taking of roentgenograms of a large group of individuals are useless and not practical, but other methods are extremely valuable, and I mean by this the recognition of the precursors of cancer. We know that gastric ulcers degenerate into cancer in about 5 per cent of our cases, that only 5 per cent of polyps account for cancer, and that so-called atrophic gastritis involving the prepyloric area of the stomach degenerates into or becomes a precursor of carcinoma of the stomach in an even smaller percentage of cases, but what about the remaining huge group of individuals? A number of factors

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will enable us to screen these persons. Age is of great value. Sex is important. In our own experience in the Lahey Clinic, for instance, 64 per cent of patients with tumors of the stomach (and that means cancer in 97 per cent of the cases) were males, and 90 per cent were past the age of 45. These are screening factors that are of great assistance to us.

What about pernicious anemia? We know from our own statistics and from the literature that the incidence of cancer of the stomach in patients with pernicious anemia may be two or three times that in a cross section of the population. We should, then, study these individuals past 45 years of age with repeated roentgenologic examinations.

Again, for screening purposes, a history of cancer in the family, particularly cancer of the stomach, is of great use to us, as is the presence of achlorhydria. If these screening factors are taken into consideration it may be possible to diagnose cancer much earlier and to obtain better results with more radical surgical procedures.

It is true that many early cancers of the stomach grow rapidly and result in early death even after resection. Cancer of the stomach spreads rapidly through several channels, and we have been accustomed to basing postoperative prognosis on involvement of the lymph nodes. There are other factors which determine the spread and the ultimate prognosis in these cases. General lymphatic spread is just as important as involvement of the lymph nodes. There is also involvement of the vascular system. Dr. W. A. Meissner in Dr. Shields Warren's laboratory found an incidence of vascular involvement of 57 per cent in cases in which there was no relation to the lymphatic involvement. We know that there is spread to the duodenum and that cancer frequently involves the muscularis and the mucosal area of the duodenum for 3 or 3.5 cm. beyond the pyloric vein. We know, too, that when there is general spread of cancer of the stomach, cancer cells can be seen growing along the nerves and approaching the serosa of the stomach. These are the rapidly growing and spreading types of tumors, and in such anaplastic lesions there may be gravitational metastases with widespread peritoneal involvement.

We have seen patients with gastric cancers who go along for years. I know of one patient who is alive five years after an inoperable, proved carcinoma was found at exploration. Such a case emphasizes the necessity for knowledge of the life history of cancer, about which we know very little. The screening methods will help considerably. The age of the individual is of help. A man past the age of 45 or 50 years who has gastrointestinal symptoms that do not respond to ordinary functional measures, diet, and so forth, should be very carefully studied by means of roentgenologic and gastroscopic examination, the Papanicolaou test and every other available method to rule out carcinoma in the stomach. Even then, if we cannot be sure and if there is suspicion of a deformity on subsequent roentgenograms, exploration should be carried out because the outlook is so unfavorable unless operation is performed early.

Let us then develop suspicion of carcinoma of the stomach. If we look for it, I am sure that many of these cases can be discovered not only when they are resectable but also when resection can be performed with a high percentage of five year survivals.

When one remembers that most patients who come to us for surgery have advanced carcinomas and that 27 per cent of those on whom we have done resections are alive and well after five years, the situation is not too hopeless. In our earlier group of total gastrectomies, 1 patient in 8 is alive and well five years after operation; this group constituted advanced, hopeless cases in which nothing else could be done short of total gastrectomy.

It should be remembered also that the majority of tumors of the stomach are carcinomas. A small group of tumors may be benign—in our own cases about 1.5 per cent. In another group the tumors arose from other tissue elements of the stomach and produced sarcomas, principally developing on lymphoid tissue and on smooth muscle tissue. Sarcomas can develop from the other mesenchymal elements of the stomach (such as vascular, nerve and fibrous tissue), but they are so rare that

they scarcely need to be mentioned.

Today we have on the platform 2 patients who were kind enough to come here. The first patient is a man 45 years of age who had been well except for a little indigestion, such as burning in the epigastrium and a little pain. His first symptom that indicated anything seriously wrong was gastric hemorrhage. His red blood cell count became fairly low and he required about eight transfusions; hemoglobin rose from 8.2 to 14 gm.

The first roentgenologic examination was not very satisfactory, and a gastroscopic study was done which showed a well circumscribed, small tumor on the anterior wall. A subsequent roentgenologic examination showed a fairly well demarcated intragastric tumor. Most such tumors are benign and in most cases a diagnosis of leiomyoma can be made.

At operation a tumor characteristic of a leiomyoma of the stomach was removed. Such tumors arise from the smooth muscle elements of the stomach, and the first symptom may be sudden onset of bleeding.

This patient tells me that he did not vomit blood but passed blood in the stool and felt weak and faint. It was noted that he was pale and had a rapid pulse. It has now been two years since this tumor was removed and this man is well. (To the patient): Is that right?

PATIENT: Yes, sir.

DR. MARSHALL: He has had no difficulty except occasionally a little indigestion. The point of great importance is that it makes little difference whether this tumor is a simple leiomyoma or a leiomyosarcoma; local extirpation in most of these cases may be sufficient even if it is sarcoma. The mucosa over these tumors becomes very thin, erodes and ulcerates, and the first symptom is massive hemorrhage. These ulcerations may be deep; I have often seen them deeper than the ordinary penetrating ulcer in the first part of the duodenum.

The history in these cases is quite characteristic. When a history is obtained such as that related by this patient, the physician should always think of the possibility of a leiomyoma or leiomyosarcoma. Because a leiomyoma cannot be distinguished roentgenographically from a leiomyosarcoma and also because many of these tumors are in the antral area of the stomach, we ordinarily do a partial resection. If they are located high in the stomach, one is justified in doing a simple operation instead of a total or major operative procedure, and this is just as safe with a sarcoma as with a nonmalignant type of tumor. If there is any recurrence, further resection should be performed, but such tumors do not metastasize early. Fortunately this patient did not have a sarcoma; he had a simple leiomyoma.

The problem of gastric cancer, which comprises about 97 per cent of the cases, is entirely different. Again, the diagnosis must be made early if anything is to be done for these patients. In many cases the good results obtained from resection depend on the type of tumor—whether it is very anaplastic, whether it is growing rapidly, and whether it is a polypoid tumor or an adenocarcinoma. Some of the best results as far as survival is concerned have been obtained in cases of adenocarcinoma. We have all seen patients with a small carcinoma simplex which involved the pyloric area of the stomach who are doing very well 5, 10 and 15 years after resection. We have also seen patients with small tumors which we thought were curable because of their size and the extent of involvement who have had recurrent tumors within a year and have had further serious difficulty very rapidly thereafter.

Our second patient had a large filling defect in the antral area of the stomach on roentgenologic examination. How old were you when you were seen by your physician?

PATIENT: Fifty-six years of age.

DR. MARSHALL: That is about the average age of patients with neoplasms of the stomach. It is well to point out also that this is about the average age of patients with simple gastric ulcer. The physician must suspect the presence of a tumor in such cases.

This patient came to the clinic here in Cleveland with a complaint of pain in the left anterior portion of the chest of two weeks' duration and swelling of the right lower leg and ankle. It was apparent that she had

chronic, old phlebitis, and perhaps some of the pain in the chest was on a functional basis owing to the marked anemia which was discovered at the physical examination. At that time the hemoglobin was 8.6 gm. The remainder of the laboratory data is of no consequence.

The original examiner suspected a tumor of the gastrointestinal tract, and a roentgenogram was obtained that showed the large filling defect which I mentioned previously.

On August 4, 1952, subtotal gastrectomy was performed and part of the stomach was removed along with the greater omentum. The pathologist reported this to be a polypoid neoplasm involving the body and vestibule, papillary in type, grade 2, with extensions to the submucosa but not to the muscularis. Secondary neoplasm was present in one of 18 lymph nodes of the greater curvature. That is not of great prognostic significance because, as I said earlier, there are other modes of spread of the tumor, not only into the lymph nodes but also through general lymphatic spread, through all the layers of the wall and between the layers, and the extent of the tumor cannot be determined from its gross appearance at the operating table.

Is it practical, then, to obtain biopsies and determine whether the resection is beyond the spread of the tumor at the time of operation? It is totally impractical, because one would have to include not only the edge of the stomach nearest to the tumor but also the whole circumference of the stomach. How, then, can we be sure that we are well beyond the ordinary microscopic distribution of the tumor by general lymphatic spread or by vascular spread? This can be assured only by more radical surgery, and that is the only answer we have today for this serious problem.

How many individuals have neoplasms of the stomach every year in this country? According to the United States Government Vital Statistics, approximately 30,000 to 35,000 individuals die each year from this disease. It must be remembered that at least three to four times that number have had operations or are living with undiscovered or inoperable neoplasms of the stomach. Therefore, when an individual has anemia that is unexplainable, a roentgenogram of the stomach should be obtained at once. The value of a roentgenogram is, of course, entirely determined by the experience of the roentgenologist. Unfortunately, so often a good roentgenogram is obtained but the interpretation is wrong. Only last week I operated on a woman who had had symptoms for a year; a roentgenogram had been obtained which was said to be negative, and another year was allowed to elapse before another roentgenologic examination was obtained. If the individual has gastrointestinal trouble and the roentgenogram is negative, roentgenologic examination should be repeated in a month and again later. The patient should have a gastroscopic examination, and if a neoplasm is even suspected, an exploratory operation should be performed. That is the only way to rule out carcinoma and to cure that individual. I would like to emphasize the importance of operation especially, since abdominal exploration is not a serious procedure. We have performed exploratory operation on more and more of these patients in order that diagnoses will be made earlier and thus early resections will be carried out.

TABLE 1

CLASSIFICATION AND INCIDENCE OF GASTRIC SARCOMA

Leiomyosarcomas		9
Lymphoid tumors		32
Hodgkin's disease	10	
Reticulum cell sarcoma	6	
Lymphosarcoma	12	
Malignant lymphoma	4	
TOTAL		41

In a study made in 1950[1] it was found that of 1,171 patients with malignant tumors of the stomach (from 1929 to 1949), 41 had sarcoma, an incidence of 3.5 per cent. The pathologic classification of this group of 41 cases is shown in Table 1. If at operation a large tumor is found which appears to be inoperable, a biopsy should be performed because a small percentage of such tumors prove to be lymphosarcoma which responds to radiation. We have had patients with Hodgkin's

disease who were alive seven or eight years after radiation in whom at laparotomy the tumor was considered inoperable.

The over-all age incidence of carcinoma of the stomach is 11 per 100,000 for ages 1 to 74 years, but the incidence between 45 and 74 years of age is about five times that for the entire age group. It should be remembered that 90 per cent of malignant tumors of the stomach occur in patients past the age of 45 years.

Delay in treating is a distressing feature of this problem. We studied 300 patients with a diagnosis of carcinoma and found that in 93 the physician was responsible for the delay. These 93 patients had had symptoms from three months to two years without even a roentgenologic examination. Many of them had been treated for various functional diseases and no special diagnostic studies had been carried out. In 118 of the 300 cases the patient was responsible for the delay in treatment. This indicates the need for education of the public in order that earlier diagnoses may be made. Of the group of 300 patients only 89 had had symptoms for less than three months.

TABLE 2

EARLIEST SYMPTOM NOTED—300 PATIENTS

	Cases
Epigastric pain or discomfort	170
Flatulence	34
Anorexia	29
Nausea or vomiting	24
Dysphagia	17
Anemia (pallor or weakness)	9
Weight loss	9
Bleeding (hematemesis or melena)	4
Abdominal mass	3
Diarrhea	1
TOTAL	300

In Table 2 are listed the earliest symptoms noted in a group of 300 patients. We must not deride patients for coming to the physician because of fear of cancer. We must not wait until they present the picture of advanced cancer, that is, until bleeding, weight loss, anemia and malnutrition are present. In our experience, epigastric discomfort—it may not even be pain but only discomfort plus anorexia—is enough to warrant very careful special examinations so that diagnoses can be made early enough for surgical treatment.

I would like to discuss briefly the precursors of carcinoma of the stomach. In a study of 600 cases of gastric ulcer by Drs. Smith and Jordan[2] at the clinic, only 270 patients underwent operation because the ulcer did not heal, because it recurred or because cancer was suspected. In 59 of the 270 cases, or about 1 in 5, the ulcer was malignant. Only a very small percentage of gastric carcinomas develop on ulcers, but just how small this percentage is we cannot say. The practical point is, can we be certain which ulcer is malignant and which is benign? The only criteria of any value are failure of the ulcer to heal, persistence of ulcer and recurrence of ulcer.

There is no unanimity of opinion as to whether or not polyps become malignant. A large percentage of those that we have removed (and we always remove them) show malignant degeneration.

In regard to resectability, in some cases it is easy at laparotomy to say that a tumor is fixed and is inoperable. In other cases operability cannot be determined by palpation at laparotomy. In such cases if the omentum is detached and the stomach turned upward, involvement of the celiac nodes, of the pancreas or of adjacent organs can be seen. If the surgeon can remove any structure that is invaded by cancer, resection should be performed: that means that more total gastrectomies are being performed and are justified because of the possible increase in survival rate and because the mortality after total gastrectomy is comparable to that of partial resection. In total gastrectomy not only all of the stomach, but also all involved adjacent organs, lymph nodes, omentum and spleen are removed.

In a group of 469 patients who came to the clinic from 1936 to 1940, inclusive, 48.2 per cent were considered inoperable; only 19.4 per cent had exploratory operations and of this group, 24.1 per cent had partial gastrectomies (Table 3). When these figures are

TABLE 3

CARCINOMA OF THE STOMACH—469 PATIENTS
(1936 to 1940 Inclusive)

	CASES	PER CENT
Inoperable—no exploration	226	48.2
Exploration and biopsy only	91	19.4
Palliative operation	39	8.3
Partial gastrectomy	113	24.1

TABLE 4

CARCINOMA OF THE STOMACH—230 PATIENTS
(1941 to 1945 Inclusive)

	CASES	PER CENT
Inoperable—no exploration	31	13.5
Exploration	102	44.3
Palliative operation	12	5.2
Resection	85	37.0
Total	18	
Partial	61	
Transthoracic	6	

compared with those shown in Table 4 (for the period from 1941 to 1945), it can be seen that 44.3 per cent of a group of 230 patients had exploratory operations and as a result resection was carried out in 37 per cent. The only treatment for carcinoma of the stomach is resection, and all patients should be given the opportunity of a radical operation unless nonremovable extragastric spread can be demonstrated.

In conclusion, we must be suspicious of the presence of cancer. Patients should be screened and special tests performed, and that means not only roentgenographic study but also gastroscopic examination and cytologic smears. If the diagnosis is made early, carcinoma of the stomach is not an incurable condition and we can do much for those patients.

REFERENCES

1. MARSHALL, S. F. and MEISSNER, W. A.: Sarcoma of the stomach. Ann. Surg. 131:824-837 (June) 1950.
2. SMITH, F. H. and JORDAN, S. M.: Gastric ulcer: A study of 600 cases. Gastroenterology 11:575-593 (November) 1948.

Postgraduate Clinical NOTES

8. THE CORE OF THE CANCER PROBLEM

The cancer problem is a problem in the behavior of living cells. Now, the living cell is a chemical machine. It lives and moves and has its being by the energy which it derives from the chemical reactions carried out within itself, using the chemicals on which it feeds as its fuel. Moreover, it renews its own structure, it keeps its machinery in good working order by repair processes which use these same foods as construction materials. Each type of cell has its own peculiar structure and its own particular functions and conducts its chemical transactions in its own unique way. If its structure or its activities change its chemical traffic will also change. If some cells of a tissue continue to grow and multiply when their neighbors have ceased to do so it is because the aberrant cells are pursuing a pattern of chemical behavior different from that of the community. A malignant cell must differ chemically from a normal cell because it behaves differently. If we are to control the growth of tumors by means other than complete removal we can do so only by controlling their chemical reactions.

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The Treatment of Burns by the Exposure Method

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THE treatment of burns by the exposure method was first reported in the United States by Copeland[1] in 1887. In 1914 this method was described in an editorial in the *New York Medical Journal*,[2] and in 1915 Haas[3] and Herrman[4] independently published favorable reports on the exposure treatment of burns. For unknown reasons, the exposure method was gradually abandoned until 1949, when it was reintroduced by Wallace.[5]

Our interest in the exposure method was stimulated by the release of information revealing the overwhelming incidence of thermal burns in atomic warfare. Several thousand burn casualties might be expected after the explosion of an atomic bomb over any large city. The possibility of such a catastrophe requires simplification of methods of treatment. With these considerations in mind, a study of the practicability and effectiveness of the exposure method was undertaken. In the past three years approximately 350 burn patients at Brooke Army Hospital have been treated by the exposure method, and it has been found that this method is not only practicable in the event of catastrophe but also worthy of consideration in the treatment of burns during peacetime.[6-8]

*From the Surgical Research Unit, Brooke Army Hospital, Fort Sam Houston, Texas.
Adapted from an exhibit shown at the annual meeting of American Medical Association, 1952.

Definitions

Eschar: Dead tissue of a full thickness burn.

Crust: Dried exudate that covers an exposed partial thickness burn.

Scab: An incrustation that forms over exposed open wounds other than burns.

What Is the Exposure Method?

The exposure method is a technic of local care of the burn wound. When a partial thickness burn is exposed, the exudate that weeps from the surface slowly dries in 48 to 72 hours and forms a hard crust that serves as a physiologic protective cover for the wound. As long as this crust is intact, it acts as a barrier against invasive infection. Epithelial regeneration occurs beneath the crust. Between 14 and 21 days after injury, the crust desquamates spontaneously and a well epithelized surface remains.

The evolution of a full thickness burn is different. Since surface exudate is minimal, crust formation does not occur. Instead, the charred or pearly-white dead skin dehydrates and is converted into an eschar which serves as a protective covering for the wound. The eschar remains essentially unchanged until spontaneous sequestration begins, which usually occurs after three or four weeks. Exposure ends in a partial thickness burn when the crust desquamates and the wound is healed; exposure ends in a full thickness burn when the eschar is excised.

The exposure method has been referred to as the open method of treatment in contradistinction to the closed method of occlusive pressure dressings. When properly applied, the exposure method is a *closed* method of treating the burn wound because the crust or eschar that naturally forms on the injured surface is a tightly adherent, physiologic dressing. Frequently, burns are permitted to remain open, but they are not positioned in a way that a protective incrustation can form over their surface. This type of treatment results in an open wound surface because contact with other body surfaces or bed clothing prevents the formation of a physiologic covering. This form of therapy must be considered *neglect*, rather than treatment by exposure.

Details of Management

Local care must be deferred until fluid and electrolyte replacement has been successfully initiated. The exposure method is carried out according to the following outline:

1. *Cleansing*—Burned areas are gently washed with a bland white soap and copious amounts of water. Intravenous morphine analgesia is sufficient. Aseptic precautions are unnecessary.

2. *Removal of devitalized epidermis*—All blisters are opened and all detached epithelium is cut away.

3. *Systemic antibiotics*—Penicillin, 1,000,000 units as an initial dose, and 300,000 units twice daily, is administered until a satisfactory incrustation is formed over the burned surface. Further antibiotic therapy is given only on specific indications.

4. *Exposure to the air*—All burn surfaces are completely exposed to the air in order to permit drying.

CASE 1 Superficial Partial Thickness (Second Degree) Burn

A 37 year old Air Force officer sustained flame burns of the face and the dorsa of both hands when he attempted to rescue several airmen from a burning building. Penicillin, 300,000 units daily, was administered for five days. The burn surfaces were cleansed with soap and water and all blisters were removed. The patient was encouraged to keep his hands elevated and in a position of function (Figure 1a, b and c).

FIGURE 1a. Three days postburn. The exudate dried in 48 hours and formed a crust on the dorsa of the hands. The hands are in excellent position, and the protective covering is intact.

FIGURE 1b. Eleven days postburn. The crust has darkened, the hands are still in a good position and the crust serves as a splint. The edema has disappeared and there is no evidence of infection.

FIGURE 1c. The crust spontaneously desquamated on the eighteenth day, and at the time of discharge there was a well epithelized surface. There was no limitation of motion.

CASE 2 — Deep Dermal (Deep Second Degree) Burn

A 21 year old Negro Air Force sergeant received burns of the hands, face, buttocks and right thigh when gasoline exploded while he was refueling an airplane. A large area on the anterior aspect of the right thigh showed a deep second degree burn. He was placed in bed so that the area remained completely exposed to the air (Figure 2a, b, c and d).

FIGURE 2a. Twenty-four hours postburn. The exudate on the surface has started to dry, but a crust has not formed. The exudate from the wound can be seen at the edges.

FIGURE 2b. Six days postburn. A good crust formed in 72 hours. By the sixth day all edema had disappeared and there was no evidence of infection.

FIGURE 2c. Twenty-eight day postburn, little crust remaining. On twenty-first day, superficial burn areas began to desquamate. Epithelization time depends on depth of second degree burn.

FIGURE 2d. Forty days postburn. The surface is well healed, without scarring.

CASE 3 Full Thickness (Third Degree) Burn

A 29 year old woman was burned on the posterior aspect of her right thigh when her housecoat ignited from an open gas stove. There was mixed partial and full thickness skin loss. The patient was placed in bed to lie on her abdomen in order that the entire burn surface could be exposed to the air (Figure 3a, b, c and d).

FIGURE 3a *(below)*. Thirty-two hours postburn. Little exudate weeps from the wound. Because of the depth of the burn the patient experienced minimal pain.

FIGURE 3b. Seven days postburn. The edema has subsided, the eschar is dry, and there is no evidence of infection at the edges of the wound.

FIGURE 3c *(above)*. Fourteen days postburn. The partial thickness area in the popliteal space is completely healed. The remaining eschar is tightly adherent.

FIGURE 3d *(below)*. Fourteen days postburn. The full thickness eschar was surgically removed with the patient under general anesthesia. A small area of crust at the distal portion of the wound was permitted to remain intact and to desquamate later. In full thickness burns the exposure method is applicable only until the eschar is removed, since granulating surfaces should not be exposed.

CASE 4

Burn of the Face

A white girl, 1 year of age, was burned when a hot water heater exploded. The burns extended over 23 per cent of the body surface. There was a deep burn on the face. Penicillin, 200,000 units daily, was given for 12 days. (Figure 4a, b, c and d.)

FIGURE 4a *(left)*. Eighteen hours postburn. Note the marked edema of the eyelids and lips. The hair has been shaved from the head.

FIGURE 4b *(right)*. Fourteen days postburn. All edema has subsided. A small area of superficial burn can be seen on the ear. The protective eschars are tightly adherent and there is no evidence of infection.

FIGURE 4d *(right)*. At the time of discharge, all the grafts have taken well and scarring is minimal.

FIGURE 4c *(left)*. Twenty-one days postburn. The eschar on the face has been removed. This was accomplished, beginning on the fifteenth day, by the use of wet dressings. Partial thickness burn areas are healed, but a large portion of the right side of the face is full thickness injury. Strips of skin 0.012 inch in thickness, taken with an electric dermatome, were placed over the denuded areas and a large, firm, bulky dressing was applied.

CASE 5

Deep Burns of the Back

A 7 year old white girl was burned when her clothes caught fire while she and some friends were playing with matches. There were deep dermal and full thickness burns over the posterior aspect of the trunk, the buttocks and the upper arms. After shock therapy the burn surfaces were cleansed and VASELINE® gauze pressure dressings were applied. The patient was then transported 75 miles to our hospital. Immediately on admission the dressings were removed and the burn surfaces were again cleansed. (Figure 5a, b, c and d.)

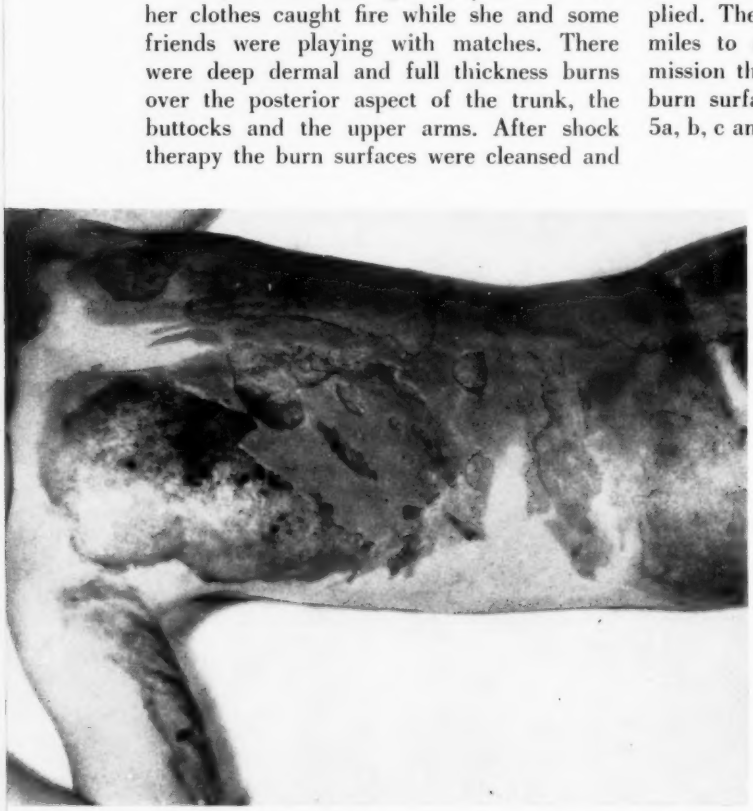

FIGURE 5a. Thirty hours postburn. After the areas had been recleansed, they were permitted to remain exposed to the air. The patient complained of being cold but experienced no other discomfort.

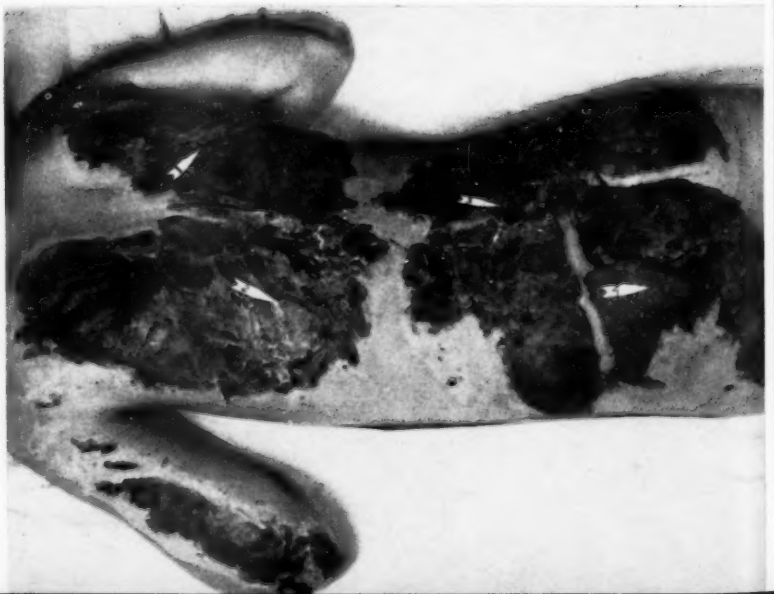

FIGURE 5b *(right)*. Thirteen days postburn. A good eschar formed over the burn surfaces in 96 hours. Partial healing of some of the more superficial areas on the arm and in the center of the back can be seen. The eschars over the full thickness burn surfaces remain intact. The child was comfortable, and there was no evidence of infection.

FIGURE 5c *(right)*. Twenty-two days postburn. The eschars were surgically removed and the clean surfaces of the full thickness injury covered with the dressings. Skin grafts were applied four days later and held in place with occlusive dressings.

FIGURE 5d. Forty-four days postburn. The thin split thickness grafts have taken. Areas of deep dermal involvement healed with little scarring.

CASE 6

Comparison of Exposure and Occlusive Pressure Dressings

A 20 year old airman sustained partial thickness burns of the dorsa of both hands when his clothing caught fire from a gasoline explosion. The burns of both hands appeared to be of approximately the same depth and extent. Both hands were cleansed with soap and water. All blisters were broken and the devitalized epithelium was cut away. Penicillin, 300,000 units daily, was given for five days. (Figure 6a, b, c and d.)

FIGURE 6a *(right)*. Thirty hours postburn. An occlusive pressure dressing was placed on the left hand, and the right hand was permitted to remain exposed to the air. The patient was encouraged to hold his right hand in a position of function.

FIGURE 6b. Nine days postburn. The dressing has been removed from the left hand. A firm protective crust has formed on the dorsum of the right hand. Infection is not evident in either hand. The left hand was placed in a position of function and redressed with an absorptive dressing.

FIGURE 6c. Twenty-three days post-burn. The crust on the right hand has desquamated from a well epithelized surface. The left hand likewise is almost completely healed with the exception of a few deeper areas on the fingers. In neither hand is infection evident. The patient stated that during the first two days of therapy the hand that was dressed was more comfortable, but throughout the remainder of his course of treatment he emphasized that the hand treated by exposure was much more comfortable than the dressed hand.

FIGURE 6d. At the time of discharge both hands had healed well. There is no evidence of scarring on either hand. Function returned to normal in approximately the same period of time in both hands.

Evaluation of Exposure

The loss of exudate from the burn wound is approximately the same with the use of the exposure method as with the use of occlusive pressure dressings.

The average healing time for second degree burns is 16 days.

Third degree burns are usually ready for grafting when the surrounding partial thickness burns are healed. Most eschars over the joints of the hand and other flexor surfaces should be excised by the eighth to the tenth day. All eschars should be excised by the twenty-first to the twenty-sixth day.

Indication for Exposure

1. All burns that can be adequately exposed and put at rest.

Contraindications for Exposure

1. Circumferential burns of the trunk.
2. Patients requiring immediate transportation.
3. Ambulatory outpatients.
4. Coexisting soft-tissue wounds.

Advantages of Exposure

1. Rapidly accomplished with minimal expenditure of effort.
2. Facilities for aseptic technic and elaborate materials for dressings are unnecessary.
3. Effective control of infection.
   a. Reduction of conversion of deep dermal to full thickness skin loss.
   b. Less grafting required; hospital time shortened.
   c. No unpleasant odor.
   d. Minimal fever, good morale.

Disadvantages of Exposure

1. Not applicable to all burns by virtue of the several contraindications.
2. Unpleasant sensation of pain and cold before crust formation.
3. Positioning of injured areas is sometimes difficult.

REFERENCES

1. Copeland, W. P.: The treatment of burns. M. Rec. 31:518, 1887.
2. Editorial: The treatment of burns. New York M. J. 99:541, 1914.
3. Haas, S. V.: The treatment of burns in children by exposure to air. Am. J. Surg. 29:61, 1915.
4. Herrman, C.: A note on the open method of treating burns. Am. J. Surg. 29:63, 1915.
5. Wallace, A. B.: Treatment of burns. Ann. Roy. Coll. Surgeons 5:283, 1949.
6. Pulaski, E. J. and others: Exposure (open) treatment of burns. U. S. Armed Forces M. J. 2:769, 1951.
7. ———: Evaluation of the exposure method in the treatment of burns. In: Surgical Forum, American College of Surgeons. Philadelphia, W. B. Saunders Company, 1952.
8. Artz, C. P., Reiss, Eric, Davis, J. H., Jr. and Amspacher, W. H.: The exposure treatment of burns. (in press.)

A Simple Method for Detecting the Salt Depletion Syndrome During Cardiac Therapy

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In the management of congestive circulatory failure a dangerous complication is the development of the low salt syndrome. The recognition of this condition is not always easy. To detect this syndrome a practical clinical method without recourse to complicated laboratory procedures is presented.

J. J. SILVERMAN

WITH the employment of diets rigidly low in salt, and with the frequent use of mercurial diuretics, a salt depletion syndrome has been observed with increasing incidence. The hazards of salt depletion have been emphasized in recent years.[1-4] Unfortunately, the recognition of this complication is not easy. The low salt syndrome has a varied clinical picture and unless the clinician is alerted to its presence it may easily escape detection. The onset is insidious; the symptoms at first are neither alarming nor serious. These patients complain of drowsiness and apathy, symptoms that may be attributed falsely to sedation or a neurosis. Anorexia, nausea and vomiting may contribute to a further decrease in the salt intake, and these symptoms may be attributed erroneously to digitalis toxicity. What is worse—even dangerous—since patients with the syndrome are often in a state of resistant heart failure, they are mistakenly subjected to increased salt restriction and further diuresis.

It is the purpose of this report to present a practical method, without recourse to complicated laboratory procedures, for alerting clinicians to the low salt syndrome. The method simply depends on observing the *response* of the urinary chlorides and the *change* in body weight following the administration of a test dose of a mercurial diuretic. Ordinarily, the diuresis obtained from mercurials results in a profuse excretion of chlorides and a loss of body weight. If, on the other hand, a depression of the urinary chloride is observed and at the same time there is a prompt gain or no loss of weight, the low salt syndrome should be strongly suspected. To test the urinary chlorides, the Fantus test[5] recently modified by Bryant and his co-workers[6] is used. The test is simple to perform, reasonably accurate and is easier than testing for sugar or albumin.

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Technic

At the start of the test the patient's weight pattern is noted and a sample of urine is obtained. The diet remains unchanged and fluids are encouraged. A test dose of 1 cc. of one of the standard mercurial diuretics is administered intramuscularly. All urine passed after this injection is collected. At the end of the test period, which is usually eight hours but may be shortened to half this time, the collected urine is measured and tested for chlorides.[4] A kit containing a test tube, a dropper, a 10 per cent solution of potassium chromate, and a 0.73 per cent solution of silver nitrate constitutes all the necessary equipment.

Briefly, the test is performed by placing 10 drops of urine in a test tube and adding 1 drop of the potassium chromate solution. A yellow-orange color is produced. To this mixture the silver nitrate solution is added drop by drop—the number of drops being counted—until the color changes to a permanent reddish brown. Each drop of silver nitrate solution required to produce this color change in the urine represents 150 mg. of chloride per liter. The average normal individual will demonstrate over 3 gm. (that is, 20 drops of the silver nitrate solution required). A patient with the salt depletion syndrome will exhibit extremely low chlorides in the urine, often as low as 150 mg. (1 drop) at the start of the test, and very little change after the completion. In fact, patients with a salt depletion syndrome respond with practically no diuresis and hardly any loss of weight or, paradoxically, they may show a gain in weight.

Discussion

The profuse renal excretion of chlorides is a characteristic of the mercurial diuretics.[7] It is generally agreed that normal patients, as well as those with edema, respond to a mercurial diuretic by the formation of an increased volume of urine containing a high concentration of chlorides. Bases are also excreted. There is a smaller increase in the output of sodium relative to chlorides, and a consistently smaller increase in the amount of potassium and calcium.[8-10] With the loss of chlorides there is a lowering of the plasma chlorides and a corresponding rise in the plasma bicarbonates. During the early stages of uncomplicated mercurial diuresis the body losses of sodium are isotonic with the serum. The plasma sodium concentration, therefore, is usually not altered at this time. With prolonged mercurial diuresis a hypochloremia characteristically develops, and this is associated with an alkalosis and hypokalemia.[11,12] The increased renal excretion of potassium probably accounts for this hypokalemia. In this state of hypochloremic alkalosis a poor response to mercurial diuretics may be encountered. The addition of ammonium chloride at this time will often enhance the diuresis and cause a marked clinical improvement.

The electrolyte derangements and management of the salt depletion syndrome, however, are not so simple. The salt depletion syndrome implies more than just a loss of chlorides. What is emphasized is the fact that in mercurial diuresis the reduction and fluctuation of the serum concentration of the chloride ion are ordinarily greater and much more sensitive than the shift of the serum concentration of sodium and potassium ions.

In order to assess the role of the various electrolytes in this syndrome, complicated and expensive laboratory equipment is required. Since this type of equipment requiring trained personnel is not generally available, the precise changes in the electrolytic balance are not followed in the average patient. The chloride determination, however, lends itself readily and conveniently to analysis. In fact, the lowering of the plasma chlorides and the failure to respond by a chloruresis following a stress dose of a mercurial are such striking features of the salt depletion syndrome that by simply testing and studying the chloride excretion one can obtain important information regarding the presence of this dangerous complication. In the presence of a profuse diuresis of chlorides with a brisk loss of weight, for example, the diagnosis of the salt depletion syndrome should be seriously doubted (Figure 1). The ineffectiveness of the mercurials in the presence of hypochloremia is, therefore, of diagnostic importance. A low

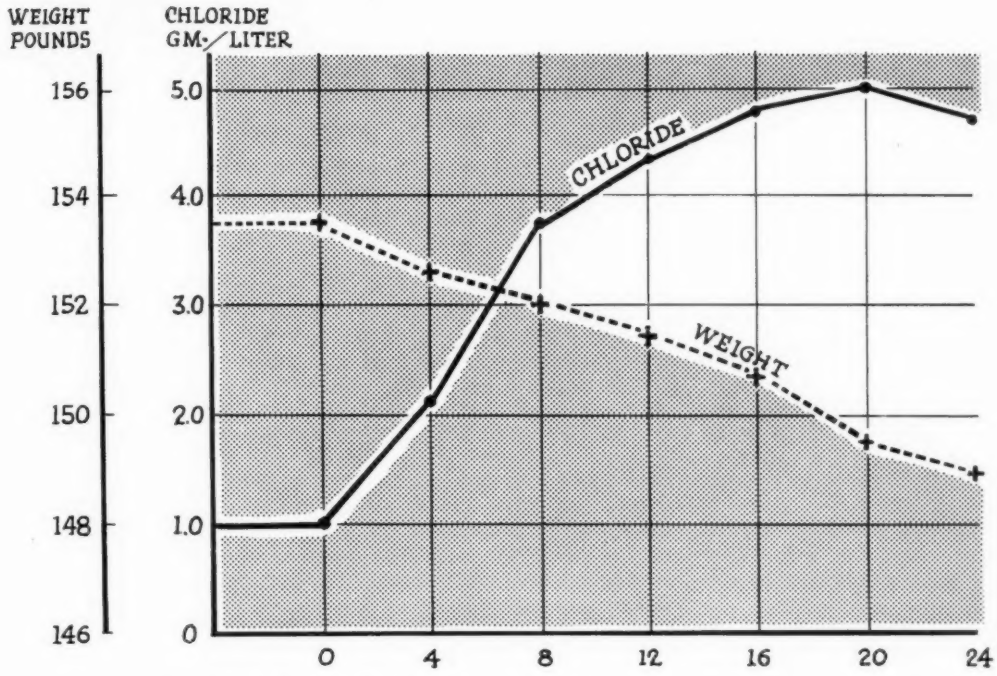

FIGURE 1. The effect of a single injection of a mercurial diuretic in a patient suffering from uncomplicated congestive circulatory failure, demonstrating the profuse excretion of urinary chlorides and loss of body weight. In the salt depletion syndrome this striking response is absent.

chloride output after a mercurial injection indicates a low concentration of this ion in the plasma.

The paradoxical phenomenon of increasing weight and edema after salt depletion is not new and has been observed by others.[13,14] According to Dock,[13] the body, in order to conserve sodium, calls forth a mechanism which initiates maximum absorption of both sodium and water by the renal tubules. Instead of calling forth a diuresis, the kidneys, in response to the stimulus of a mercurial diuretic, seem unable to excrete sodium and water.[15-17] Since the dietary sodium is restricted and water is available, the extracellular fluid becomes relatively hypotonic. Fluid is then attracted to the intracellular space because of its relatively high electrolyte concentration. As a result of these changes, weight increases, there is a diminution in the effective renal glomerular flow, and azotemia develops.

It should be emphasized that this method for screening patients for the salt depletion syndrome has certain pitfalls. In the first place the test emphasizes chloride excretion, and since the losses of sodium and potassium must be reckoned with in therapy consideration of these vital ions must not be neglected. A refinement of the test consists of studying the urinary *p*H, and for clinical purposes this can be performed simply by using nitrazine paper.[18] If the diuresis is mainly one of chloride without a proportionate loss of sodium and potassium the urine will be acidic with a *p*H of 5.5 to 6.5. A *p*H above 7.5 suggests that there are more base ions than chloride ions lost in the urine. If the *p*H is neutral the results are equivocal. By this method it is possible to gain some insight in deciding whether one is dealing with a hypochloremic alkalosis or a hypochloremic acidosis. It is impossible from this method to differentiate between the potassium and sodium losses.

Electrocardiographic studies, however, may be of value. It is rare for the electrocardiogram and the serum potassium to be normal in the presence of frank potassium depletion. In the presence of low concentration of serum potassium, the electrocardiogram may demonstrate low, flat T waves, depression of the RS-T segment and prolonged Q-T intervals.[19] Unfortunately, these changes may be obscured by digitalis or previous myocardial damage.

Another pitfall of the test is the assumption that the amount of sodium lost can be calculated accurately from the amount of chlorides excreted in the urine. This error is based on the fact that chlorides traditionally are expressed in terms of sodium chloride. In a normal individual consuming an average diet, this error is small since the amounts of sodium and chlorides are proportionately the same. However, specially prepared diets rich in chlorides and containing salt substitutes are unequal in their sodium content and consequently lead to a disproportionate loss of chlorides in the urine. Similarly, patients who are consuming ammonium chloride and cation exchange resins will demonstrate a proportionately high concentration of chlorides in the urine. The test may also be unreliable immediately following major operative procedures.[20] It should be pointed out that the test of an extremely dilute urine, such as might be encountered in a casual specimen, should be interpreted with caution. Finally, the test is unreliable in the nephrotic syndrome, in some of the organic nephropathies and in Addison's disease.[21]

In spite of these limitations, the technic proposed can be applied to most cardiac patients who are on a low salt diet and who are receiving mercurial diuretics. It is not the purpose of this paper to discuss the management of the salt depletion syndrome, but merely to point out a method by which the clinician can be warned of its presence. Once the suspicion of a salt depletion syndrome has been strengthened such factors as the degree of acidosis, hypokalemia and azotemia must be considered. As stated previously, mercurial diuresis at first causes a hypochloremia without changing appreciably the blood sodium concentration. This is the early phase of the salt depletion syndrome and is often associated with so-called mercury fastness. Later this chloride depletion is followed by a lowering of the bases in the cells and blood. This stage of the salt depletion syndrome is the more serious one. Not only chlorides but also sodium and potassium must be supplied. It is interesting to note that a lowering of the blood electrolytes may occur quite independently of diet and diuretics. In fact, the salt depletion syndrome may be a nonspecific manifestation of the dying stage.[22] Obviously, the management of patients with the salt depletion syndrome is complex, and many of the physiologic derangements encountered are not completely understood.

It is surprising how infrequently the urine of cardiac patients is examined for chlorides. Since many of these patients are on a low salt diet, and often are receiving mercurials, the study of the urinary chlorides becomes increasingly important. Now that a convenient method is available, the study of the pattern of the daily chloride excretion, like the daily weight, should be more widely practiced. Testing for urinary chlorides is easier and less expensive than is testing for sugar. No complicated laboratory equipment is necessary; the test can be carried out in the home or in the office. Over the past few years this type of testing has been found to be extremely rewarding, particularly in the elderly arteriosclerotic and hypertensive patient.[23] By simply observing the pattern of chloride excretion and weight change, important information regarding the salt depletion syndrome can be obtained.

Summary

A simple clinical method for alerting the clinician to the salt depletion syndrome is presented. The method depends on observing the response of the urinary chlorides and the change in body weight following a test dose of a mercurial diuretic.

In managing cardiac patients on a low salt diet and mercurial diuretics, testing the urine daily for chlorides yields important clinical data and should be more widely practiced.

REFERENCES

1. Schroeder, H. A.: Renal failure associated with low extracellular sodium chloride. J.A.M.A. 141:117, 1949.
2. Soloff, A. and Zatuchni, J.: Syndrome of salt depletion. J.A.M.A. 139:1136, 1949.
3. Citron, D., Bercu, B., Lemmer, R. and Massie, E.: Congestive heart failure and hyponatremia: Untoward effects of mercurial diuresis. Ann. Int. Med. 34:872, 1951.
4. Marriott, H. L.: Water and Salt Depletion. Springfield, Illinois, Charles C Thomas, 1950.
5. Fantus, B.: Fluid postoperatively. J.A.M.A. 107:14, 1936.
6. Bryant, J. M., Ion, V., Phillips, C. L. and Blecha, E. E.: Estimation of urinary sodium. J.A.M.A. 140:670, 1949.
7. Schroeder, H. A.: Studies on congestive circulatory failure. IV. The effect of various diuretics on the excretion of water and chlorides. Circulation 4:87, 1951.
8. Blumgart, H. L., Gilligan, D. R., Levy, R. C., Brown, M. G. and Volk, M. C.: Action of diuretic drugs. I. Action of diuretics in normal persons. Arch. Int. Med. 54:10, 1934.
9. Blumgart, H. L., Gilligan, D. R. and Volk, M. C.: Action of diuretic drugs. II. Effect of diuretic drugs on the acid-base equilibrium of the blood in patients with cardiac edema. Medical Papers dedicated to Henry Asbury Christian (Baltimore, Waverly Press, Inc., 1936), p. 191.
10. Herrmann, G. and Decherd, G. M.: Further studies on the mechanism of diuresis with especial reference to the action of some newer diuretics. J. Lab. & Clin. Med. 22:767, 1937.
11. Friedberg, C. K.: Medical progress: Electrolyte and fluid disturbances in congestive heart failure. New England J. Med. 245:812, 1951.
12. Schwartz, W. B. and Wallace, W. M.: Observations on electrolyte balance during mercurial diuresis in congestive heart failure. J. Clin. Investigation 29:844, 1950.
13. Dock, W.: Use of sodium depletion in therapy. Advances Int. Med. 4:273, 1950.
14. McLester, J. S. and Holley, H. L.: Salt depletion syndrome with increasing edema occurring during mercurial diuretic therapy. Ann. Int. Med. 36:552, 1952.
15. Burnett, C. H.: Effects of alkalosis on renal function and electrolyte metabolism. Bull. New England M. Center 12:25, 1950.
16. Burnett, C. H., Burrows, B. A. and Commons, R. R.: Studies of alkalosis: Renal function during and following alkalosis resulting from pyloric obstruction. J. Clin. Investigation 29:169, 1950.
17. Weston, R. E. and Escher, D. J. W.: Analysis of unresponsiveness to mercurial diuretics observed in certain patients with severe chronic congestive failure. J. Clin. Investigation 27:561, 1948.
18. Bland, J. H.: The Clinical Use of Fluid and Electrolyte. Philadelphia, W. B. Saunders Company, 1952.
19. Darrow, D. C. and Pratt, E. L.: Fluid therapy: Relation to tissue composition and the expenditure of water and electrolyte. J.A.M.A. 143:432, 1950.
20. Randall, H. T., Habif, D. V. and Lockwood, J. S.: Sodium deficiency in surgical patients and failure of urine chloride as a guide to parenteral therapy. Surgery 28:182, 1950.
21. Moyer, C. A.: Fluid Balance. Chicago, The Year Book Publishers, Inc., 1952.
22. Proger, S. and O'Connor, J. J.: Intractable heart failure. Ann. Int. Med. 33:1349, 1950.
23. Jaffe, H. L., Master, A. M. and Dorrance, W.: The salt depletion syndrome following mercurial diuresis in elderly persons. Am. J. M. Sc. 220:60, 1950.

Postgraduate Clinical NOTES

9. CAUSES OF SODIUM DEPLETION

Dietary deficiency of sodium is not in itself a sufficient cause of serious sodium depletion, though it may aggravate depletion produced in other ways. Cation exchange resins are likewise ineffective in producing sodium depletion, for they do little more than prevent the absorption of dietary sodium; when cation exchange resin is added to a sodium-free diet, the excretion of sodium in the stools is not significantly increased (Mateer, et al., 1951). Clinically significant sodium depletion arises only when loss of sodium from the body is abnormally great. In the tropics, and in mines and stoke-holds, the necessities of thermo-regulation impose a loss of sodium in the sweat which may suffice to bring about either acute or chronic sodium depletion in otherwise fit people. In disease, sodium depletion arises either from external loss of gastrointestinal secretions or from increased urinary excretion of sodium. The various gastrointestinal secretions contain about 1000 mEq. of sodium per day, which represents about a third of the total sodium content of the body, and is five times as great as the average dietary intake of sodium. The stools normally contain less than 10 mEq. of sodium per day; reabsorption of alimentary tract sodium is carried out with an efficiency comparable to that of the renal tubule. Whenever appreciable amounts of gastrointestinal secretions are lost to the body, the risk of sodium depletion arises; such losses may come from vomiting or diarrhea, from fistulas, or from continuous aspiration.

D. A. K. Black. *The Lancet*, February 14, 1953, p. 305

Pediatrics IN GENERAL PRACTICE

The Newer Drugs and Their Indications in Childhood

For general practitioners, who handle more than 85 per cent of all pediatric care, POSTGRADUATE MEDICINE *here presents authoritative, up-to-date summaries by specialists in pediatric problems.*

E. PERRY CRUMP*

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THE unrelenting search for specific therapeutic agents has grown more intensive in recent years. In the special area of bacterial infection, probably the greatest advances have been witnessed. In this maelstrom of progress, new drugs have been introduced so rapidly that the practicing physician has been overwhelmed in the matter of selection, and even those engaged in teaching and research have found it impossible to keep fully abreast except in restricted specialized areas. With widespread use of these agents, disappointments have mounted because previous high claims of efficacy have been shattered by the impact of new knowledge gained through careful laboratory and clinical trial.

The indications for the newer drugs in treating childhood diseases differ from those in adults only in such general matters as details of dosage, mode of administration, etc., except in the case of those diseases especially peculiar to the pre-adult period. It is apparently safe to say that drug dosage in children still operates largely on an empiric basis and has a wide range of application from one clinic to another. This discussion cannot embrace all the newer drugs directed to the treatment of infants and children, and must therefore be restricted to but a few of those most commonly used and of accepted value.

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Antimicrobial Drugs

Choice of antibacterial agent—Faced with the problem of infection in an infant or child, one is justified in initially using combined therapy (penicillin-sulfonamide, penicillin-streptomycin, etc.) until the pathogen has been checked, not necessarily for identity but for in vitro sensitivity. For the practicing physician, even this is not always possible in the home. He must therefore be guided by clinical response, and this gives him additional cause for employing multiple therapy, particularly in severe disease. Alexander[1] emphasizes the observation that it is now apparent that each of the antibacterial agents developed during the past 10 years is limited in its capacity to overcome infections caused by

susceptible organisms if the disease is sufficiently severe. She suggests that in severe infections in which the bacterial population is presumably large, there are clear indications for employing simultaneously at least two effective agents which act through different mechanisms.

In a practical way the governing principles of rational antibiotic therapy and chemotherapy insist on attention to the following:[2]

1. Use of those chemicals or antibiotics to which the infecting organism is sensitive.
2. Administration of the drug so that it comes in direct contact with the infecting organism.
3. Determination of dosage so that the concentration of the drug at the site of the infection is adequate for the exercise of the usual bacteriostatic or bactericidal action.
4. Continuation of therapy until the infection is overcome.
5. Exercise of adequate precaution to anticipate, recognize and forestall the progress of toxic side reactions.

Failures in therapy with these drugs are probably more closely related to failure to observe the aforementioned principles than to anything else.

Bacteriologic identification of the invading organism, though important, is not usually necessary for the wise selection of the drug of preference. It is only necessary to know initially which of the available drugs will offer the greatest in vitro inhibition to growth of the organism. This can usually be determined satisfactorily within 12 to 24 hours by streaking a blood agar plate with the infected sample, seeding the plate with Difco Bacto Sensitivity Disks,* and placing in an incubator at 37° C. Within 8 to 24 hours a clear zone of bacterial growth inhibition surrounding the disks (Figure 1) will indicate the drug or drugs of choice. Criticism has recently been directed at this and other methods used in determining bacterial sensitivity. In defense of the method it can be said that it is a practical and simple qualitative guide to distinguish between susceptible and resistant organisms, and that clinical results have in general correlated closely with in vitro findings.

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Antibiotics

The so-called broad spectrum antibiotics, AUREOMYCIN®, terramycin and chloramphenicol, are active against both gram-positive and gram-negative bacteria, as well as against rickettsiae, spirochetes and certain of the larger viruses.

Recent reports of fatal aplastic anemia following the use of chloramphenicol have thrown a wave of fear into the application of this otherwise effective drug. Although it is the drug of choice in typhoid fever, and is equally as valuable in numerous infections, chloramphenicol is deliberately relegated to a temporary position of second choice (see Table 1), and probably should not be used at all until its role, if any, in the pathogenesis of fatal anemia is clarified.

Tabulations or practical guides representing specific clinical areas of usefulness of antimicrobial drugs must be perused with consideration for many important variables such as host resistance, population and virulence of the bacterial colony, age and size of the patient, drug dosage employed, etc. Because such variables, from a practical standpoint, are increased in childhood and must in

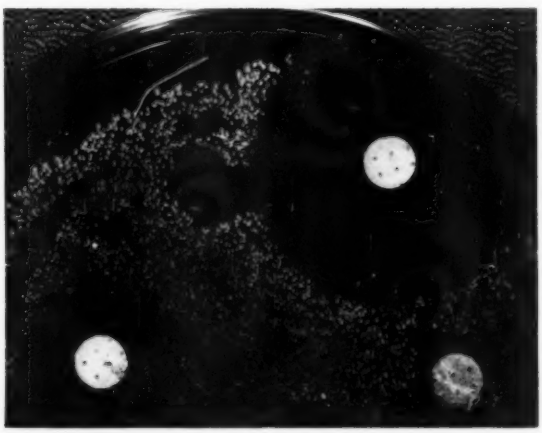

FIGURE 1. Bacterial sensitivity test after 24 hours. Note sharp, clear, circular zone of growth inhibition of bacterial colonies by terramycin disk in upper right.

TABLE 1

General Guide for Selection of Drug of Choice in Various Infections

Organism or disease	Location and/or disease process	Drug of choice	
		First	*Second*
Streptococcus (beta hemolytic)	Respiratory tract (including scarlet fever and otitis media), meningitis, empyema, arthritis and cellulitis	Penicillin	Aureomycin or terramycin
	Rheumatic fever	Penicillin*	Sulfonamide†
Pneumococcus	Lungs, meninges, endocardium, pleural and serous cavities other than meninges	Penicillin, aureomycin or terramycin	Chloramphenicol‡
Meningococcus	Meninges, septicemia	Sulfonamide†	Penicillin
Tuberculosis	Meninges, miliary, etc.	Streptomycin plus PAS plus dihydrostreptomycin	Isonicotinic acid hydrazide§
Hemophilus influenzae	Meningitis, laryngotracheobronchitis, pneumonia	Sulfonamide† plus terramycin Sulfonamide† plus aureomycin	Streptomycin Sulfonamide† plus chloramphenicol
Staphylococcus	Meninges, lungs, bone, endocardium, skin; septicemia	Penicillin, streptomycin or aureomycin	Terramycin or chloramphenicol
Rickettsiae	Murine, epidemic and scrub typhus, Rocky Mountain spotted fever, rickettsialpox	Terramycin or aureomycin	Chloramphenicol
Gonococcus	Eye, urethra, joints, etc.	Penicillin	Aureomycin, terramycin, streptomycin or chloramphenicol
Syphilis	All locations	Penicillin	Aureomycin, terramycin or chloramphenicol
Tularemia	All locations	Streptomycin	Aureomycin or terramycin
Pertussis		Terramycin or aureomycin	Streptomycin or chloramphenicol
Amebiasis	All locations	Terramycin or aureomycin	
Tetanus, diphtheria	All locations	Penicillin plus antitoxin	
Primary atypical pneumonia	Lungs	Aureomycin or terramycin	
Typhoid	All locations	Chloramphenicol	
Pseudomonas aeruginosa (Bacillus pyocyaneus)	Urinary tract, meninges, septicemia	Aureomycin plus streptomycin or terramycin plus streptomycin	Sulfonamide† or chloramphenicol
Endamoeba coli, Aerobacter aerogenes	Urinary tract, peritonitis, meningitis, septicemia, diarrhea	Aureomycin plus streptomycin or terramycin plus streptomycin	Sulfonamide† or chloramphenicol
Salmonella	Gastroenteritis	Terramycin	Streptomycin
Bacillary dysentery		Sulfonamide† or terramycin	Streptomycin or chloramphenicol
Brucellosis		Aureomycin plus dihydrostreptomycin	Streptomycin, terramycin or chloramphenicol

*For prophylaxis against recurrent streptococcal infections of the respiratory tract.

†Sulfadiazine; gantrisin; triple sulfonamides.

‡Chloramphenicol is placed in a secondary category until its role in fatal aplastic anemia is clarified.

§Can be effectively combined with streptomycin in tuberculosis.

many instances represent intangible factors. Table 1 and other similar tables are presented with the admonition that these limitations be kept in mind.

Terramycin and aureomycin—It will be noted that aureomycin and terramycin have a multiplicity of similarities in application, and may be used interchangeably in many diseases. Both are of low toxicity in children (nausea, vomiting or diarrhea), and such reactions as may occur may be largely reduced by ingestion of milk or sodium bicarbonate following each dose of the medication. These drugs should not be combined with penicillin because it appears that due to antagonism rather than synergism, the net value of the combination is significantly less than when either drug is used alone.

Both drugs reduce the severity of symptoms in pertussis, and terramycin will cure about 85 per cent of children with pinworm infection when administered three times daily for one week in doses of 10 mg. per pound of body weight. Terramycin orally has proved of value in the control of the chronic pulmonary infections in cystic fibrosis of the pancreas. Small doses (10 to 15 mg. per pound) over long periods are effective. Aureomycin is efficacious in the treatment of peritonitis or abscess complicating appendicitis in children, and has produced dramatic results in some virus infections heretofore refractory to drug therapy. Except where therapeutic effect has been striking and decisive, reports on the usefulness of antimicrobial agents have varied widely in many instances. It is difficult to calibrate the precise value of these drugs because of the multitude of factors contributing to the erratic nature of infectious disease, particularly in infants and small children.

Penicillin—Prevention of recrudescences in rheumatic fever, effectively demonstrated with sulfonamides, can be more satisfactorily achieved with penicillin. BICILLIN®,* a new long-acting repository penicillin, when given in doses of 1,250,000 units intramuscularly will apparently afford protection from streptococcal infection for more than two weeks.[3] Orally, in doses of 50,000 to 100,000 units twice daily, the same results are obtained with virtually no toxic effects. In scarlet fever and diphtheria, penicillin will quickly clear the throat of pathogens in both disease and carrier states. Congenital syphilis responds completely, and without relapse, in practically every case when penicillin is given in doses of 200,000 units per kilogram of body weight divided over a period of 21 days.

Crystalline penicillin in aqueous solution, given in massive doses parenterally (500,000 to 1,000,000 units intramuscularly) every two or three hours, is as effective in pneumococcal meningitis as is any other drug or combination of drugs. Parenteral and aerosol penicillin combined with an antihistaminic drug and penicillin nose drops have given very satisfactory results in chronic sinobronchitis in children,[4] while penicillin aerosol combined with streptomycin has given promising results in bronchiectasis.[5]

Miscellaneous antibiotics—Polymyxin B, neomycin, etc. should not be used internally except in the most desperate situations, and only after the usual toxic effects have been carefully weighed against any advantage to be derived from the drug.

MAGNAMYCIN®, ERYTHROCIN® and other very new antibiotics appear useful, but critical evaluation must await more extensive clinical trial.

Local antibiotic therapy in pyogenic infections has been highly successful with the employment of bacitracin, neomycin, polymyxin B, terramycin and aureomycin, either singly or in combination. The initial response in severe infantile eczema is considerably improved when these drugs are added to the usual local antipruritic regimen.

Dosage, in general, should be proportional to the severity of the infection. Although terramycin seems to be somewhat more effective than aureomycin weight for weight, for practical purposes dosage can be considered to be the same for both. The range of oral dosage for these drugs is 10 to 25 mg. per pound of body weight daily. For penicillin a satisfactory scale is 6000 to 12,000 units per pound of body weight per 24 hours for patients weighing less than 40 pounds, and

*N,N¹ dibenzylethylenediamine dipenicillin G; Wyeth, Inc.

TABLE 2

PRACTICAL GUIDE TO ANTIBIOTIC THERAPY
(24 HOUR DOSAGE)

AGE	PENICILLIN* (Intramuscularly†)	AUREOMYCIN AND TERRAMYCIN	
		(Orally)	(Intravenously)
Newborn	50,000- 75,000 units	75-175 mg.	40-100 mg.
6 months	100,000-200,000 units	0.175-0.425 gm.	0.1-0.25 mg.
2 years	175,000-300,000 units	0.275-0.75 gm.	0.165-0.5 mg.
5 years	300,000-400,000 units	0.5-1.0 gm.	0.25-0.6 mg.
10 years and older	300,000-400,000 units	1.0-2.0 gm.	0.6-1.5 mg.

*Same total dosage for both soluble and insoluble penicillin.

†Therapeutic oral dosage is five times greater than parenteral.

300,000 to 400,000 units per 24 hours for patients weighing more than 40 pounds (Table 2).

Antituberculous Drugs

Combined streptomycin therapy has proved superior to treatment with streptomycin alone, and is indicated when treatment must be continued for more than three weeks. Most observers report the development of resistance in over half the patients treated only with streptomycin after 90 to 120 days. Para-aminosalicylic acid (PAS) markedly reduces the emergence of such resistant strains. A controlled study by the British Medical Research Council[6] of tuberculous patients on combined PAS and streptomycin therapy revealed that 9 out of 10 of those with positive cultures had sensitive organisms after six months, as compared with only 2 out of 10 on streptomycin alone.

The daily dosage scale for PAS is 0.1 gm. per pound of body weight orally, for isonicotinic acid hydrazide 1 mg. per pound, for streptomycin 20 mg. per pound (maximum daily dose of 1 gm.) and a maximum of 25 mg. of streptomycin when administered intrathecally in children. From these approximate values it is possible to formulate an age-weight dosage table as a practical guide to therapy (Table 3).

Combined therapy employing streptomycin and PAS is of well established value in miliary and meningeal tuberculosis, and recently it has been suggested that isonicotinic acid hydrazide be added. About 10 per cent of patients treated with large doses of streptomycin develop vestibular damage early, and hearing loss much later. By contrast dihydrostreptomycin causes severe deafness early and affects vestibular function late. A very recent report[7] (Table 4) presents evidence that combining these two drugs causes dramatic reduction in the incidence of eighth nerve damage, without impairing the therapeutic effectiveness of either.

TABLE 3

AGE-WEIGHT DOSAGE SCHEDULE FOR ANTITUBERCULOSIS DRUGS

AGE (Years)	WEIGHT (Pounds)	STREPTOMYCIN		PAS	ISONICOTINIC ACID HYDRAZIDE
		Intramuscularly	Intrathecally		
1-4*	22-41	0.5 gm.	25 mg.	2-4 mg.†	22-41 mg.†
5-9	42-65	0.8 gm.	25 mg.	4.5-6.0 gm.	42-65 mg.
10-15	70-125	1.0 gm.	25 mg.	7-12 gm.	70-120 mg.

*Under this schedule, infants and small children receive proportionately more streptomycin daily.

†Orally.

TABLE 4

TOXIC REACTIONS OBSERVED WITH ANTITUBERCULAR THERAPY

(FROM HECK, W. E. AND HINSHAW, H. C.[7])

TOXICITY	STREPTOMYCIN*	DIHYDROSTREPTOMYCIN*	MIXTURE OF STREPTOMYCIN AND DIHYDROSTREPTOMYCIN†
Vestibular	27.6 per cent	7.4 per cent	0
Auditory	6.3 per cent	19.9 per cent	0

*1.0 gm. daily for 120 days.

†0.5 gm. of each daily for 120 days.

In tuberculosis, Lincoln[8] states that streptomycin is mandatory in the miliary, meningeal, protracted hematogenous, progressive primary (with cavitation and bronchogenic spread) and progressive advanced chronic pulmonary forms of the disease.

The Sulfonamides

The general indications for use of sulfonamides in diseases of childhood are well understood. It should be emphasized, however, that because of the relative inability of the infant's kidney to excrete solids, particularly during the newborn period, one must exercise caution with these drugs. It is entirely conceivable that harmful effects may result from excessive accumulation of the drug in the body fluids behind this renal barrier, especially during dehydrating episodes of vomiting or diarrhea. Sulfonamides may be readily combined with other antimicrobial agents in infection, and usually with definite therapeutic or prophylactic advantage. Sulfadiazine and GANTRISIN® are the drugs of choice, the latter because of its high solubility in decidedly acid urine and freedom from crystalluria. Triple sulfonamide compounds (without sulfathiazole) provide the same advantage, with possibly less chance of drug toxicity.

The Antihistaminics

This tremendous group of drugs have demonstrated great supportive value, but inasmuch as the basic mechanism responsible for allergic symptomatology is unaffected, they offer little in the way of curative benefit in allergic disease. The most satisfactory results are achieved in hay fever and acute urticaria, and in relieving pruritus and excessive nasal and lachrymal secretions. The excessive itching in chickenpox is often ameliorated, although these drugs offer little or no lasting benefit in eczema. Because of an atropine-like drying effect on respiratory secretions, antihistaminics are labeled by some allergists as harmful or dangerous in asthma. For continued relief, administration of the drug usually must be constant. If side reactions such as drowsiness, nervousness, etc., are too pronounced, another drug should be selected. Among the more reliable antihistaminics (CHLOR-TRIMETON®, PYRIBENZAMINE®, NEOHETRAMINE®, BENADRYL®, THEPHORIN®), no one drug is decidedly superior to the other, for it is common for a child to react either favorably or unfavorably to one and not at all to the other.

Stoesser's[9] findings in the study of 4,714 allergic children treated with 15 different antihistamines coincide generally with those of others (Table 5). Variations in percentage of improvement reported by various authors are undoubtedly dependent on the erratic, uncertain response of many children to the drugs.

Endocrine Substances

Cortisone and corticotropin (ACTH), though severely limited in curative value, are of great benefit in providing symptomatic remissions in critically ill children. Indications for ACTH or cortisone in clinical practice are limited to those entities requiring replacement of a hormonal deficiency, or conditions in which it is desirable to block severe manifestations of disease (Tables 6 and 7) despite the fact that the basic pathologic process will remain unaffected.

Dosage—Adequate dosage seems to be related more to severity of illness than to age, body weight, surface area, etc. Therefore infants and small children require proportionately larger doses than adults, and this is determined somewhat empirically. It is important, however, to attempt to utilize the smallest dose affording a therapeutic effect. The simplest laboratory test available to determine whether a satisfactory response of the adrenal gland has been obtained with corticotropin is to perform an initial direct blood eosinophil count in the fasting state, administer 25 mg. of ACTH intramuscularly, and repeat the count four hours later. A drop of 30 to 50 per cent in the eosinophil level indicates a satisfactory response. Such a patient will in most instances safely withstand the stresses of general anesthesia, major surgery, etc. If after one to three days the initial dose of ACTH has not been effective, stepladder increases may be made daily. Later, to avoid harmful withdrawal symptoms, dosage should be decreased in a like manner.

Initial requirements of ACTH or cortisone in severe situations may be twice the size of the tabulated doses in Table 8, but generally can be reduced in one to three days.

Recently a highly purified long-acting ACTH preparation* in gelatin has been developed which can be administered once daily or even less often in smaller doses with good results.

*HP ACTHAR GEL®, The Armour Laboratories, Chicago, Illinois.

TABLE 5

RESULTS OF ANTIHISTAMINIC TREATMENT OF ALLERGIES (4,714 CHILDREN)*

DISEASE	NUMBER OF CASES	SATISFACTORY RESULTS (*Per Cent*)
Urticaria-angioedema	204	88
Allergic rhinitis	2,436	67
Conjunctivitis	74	57
Hay fever	964	53
Gastrointestinal allergy	31	42
Migraine	71	31
Atopic eczema	255	28
Asthma	526	18

*From Stoesser, A. V.[9]

TABLE 6

SOME CONDITIONS IN WHICH ACTH AND CORTISONE ARE OF VALUE

- Hypersensitivities
  - Severe bronchial asthma
  - Drug reactions
  - Allergic dermatoses
- Collagen diseases
  - Rheumatic fever (acute)
  - Rheumatoid arthritis
  - Lupus erythematosus (early)
  - Dermatomyositis
- Nephrosis
- Idiopathic hypoglycemia
- Blood and lymphatic disorders
  - Leukemia
  - Lymphomas
  - Aplastic anemia (early)
  - Thrombocytopenic purpura
  - Hemolytic anemia (acquired)
- Adrenogenital syndrome
- Ulcerative colitis
- Surgery
- Burns

TABLE 7

CONDITIONS IN WHICH ACTH AND CORTISONE ARE CONTRAINDICATED

- Septicemia
- Peritonitis
- Tuberculosis (any stage)
- Diabetes mellitus
- Cushing's syndrome
- Chronic nephritis
- Marked behavior disorders
- Sickle cell anemia
- Hypertension

Rheumatic fever—In the acute episode of rheumatic carditis these drugs may prove lifesaving. Either drug will dispel the fever, polyarthritis, tachycardia, abnormal P-R interval and elevated blood sedimentation rate, usually within 5 to 12 days. Because of this power to suppress clinical manifestations without altering the underlying pathologic process in severe disease, it has been said that ACTH has enabled the patient to walk to the autopsy table.

The nephrotic syndrome—Ten to 20 mg. of

TABLE 8

GENERAL DOSAGE GUIDE FOR ACTH AND CORTISONE THERAPY

AGE (Years)	ACTH (Intramuscularly*)	CORTISONE (Intramuscularly†)
Birth to 4	10-20 mg. (2.5-5.0 mg. q.i.d.)	20-40 mg. once daily
5-9	30-50 mg. (7.5-12.5 mg. q.i.d.)	50-80 mg. once daily
10-16	60-100 mg. (15-25 mg. q.i.d.)	100-200 mg. once daily

*Intravenously, only about one-fifth the intramuscular dosage is required when ACTH is dissolved in 500 to 1000 cc. of 5 per cent glucose solution and given during an 8 to 12 hour period.

†Orally, the intramuscular dose is divided into four parts and given at six hour intervals with equal effectiveness and more rapid but less prolonged action.

ACTH dissolved in 500 cc. of 5 per cent glucose solution and administered intravenously over a period of 8 to 12 hours on six successive days will provide a satisfactory diuresis in 8 out of 10 children with nephrosis. Diuresis usually begins a few days after withdrawal of the drug.

Adrenal insufficiency—While ACTH is without effect, cortisone is of considerable value as replacement therapy in Addison's disease, and is also effective in some cases of acute adrenal failure (Waterhouse-Friderichsen syndrome).

Idiopathic hypoglycemia—McQuarrie and his associates[10] have shown that this condition (nonaddisonian type) may be regularly controlled with relatively small doses of ACTH in much the same manner that insulin controls diabetes.

Inflammatory ocular disease—In the less severe cases, particularly with anterior chamber involvement, one drop of a suspension of cortisone acetate (25 mg. per cubic centimeter) is effective when administered into the eye three to six times daily. Systemic administration is required in more extensive involvement, and the more fulminant the inflammatory lesion the larger the quantity of ACTH or cortisone necessary.

Miscellaneous Drugs

Enzymatic debridement—Favorable reports are available regarding the value of enzymatic digestion of fibrinous and purulent exudates with streptokinase and streptodornase. These substances have proved useful in the treatment of various types of empyema, hemothorax, fibrinous peritonitis and meningitis, chronic maxillary sinusitis, infected wounds, etc., during the stage when fibrinous, thick purulent exudates and blood coagula are present. They are useless, however, following the appearance of fibrous scar tissue. The enzymes, in vials containing 100,000 units of streptokinase and 25,000 units of streptodornase, may be diluted with 10 cc. of distilled water prior to injection. These substances are at present undergoing important clinical trial and are to be regarded as useful adjuncts to be combined with well established modes of management.

Vitamins—Megaloblastic anemia in infants has focused anew attention on vitamin B_{12}, vitamin C and folic acid (pteroylglutamic acid). May and his co-workers[11,12] believe that a folic acid deficiency is the primary cause of this anemia and suggest that in cases of severe or prolonged infections it is probably wise to give prophylactically added vitamin B_{12} and folic acid, inasmuch as infection, ascorbic acid deficiency and many other pathologic circumstances lead to increased requirements for vitamin B_{12} and folic acid. In the presence of megaloblastic anemia it is suggested that 200 mg. ascorbic acid, 15 mg. folic acid (pteroylglutamic acid) and 2 cc. crude liver extract (intramuscularly) be administered daily. Response is usually dramatic.

Vitamin B_{12} as a growth-promoting agent is still open to serious question and should not be used empirically for this purpose in premature or normal infants and children.

Hyaluronidase—If one desires to administer fluid, electrolytes or calories to a child when neither the oral nor the intravenous route is available, the use of hyaluronidase

makes it possible to infuse fluids as painlessly and as rapidly by hypodermoclysis as by the intravenous route. This mucolytic enzyme is useful also in other ways, especially in infants and small children. For example, it is effective in the administration of plasma by subcutaneous clysis, in intramuscular dye injections for pyelography, in increasing the area of local anesthesia in surgery and ophthalmology, and in infiltrative anesthesia for dental surgery, tonsillectomy, ankle sprains and myositis. Sensitivity rate and toxicity are negligible. Hyaluronidase is contraindicated for direct injection into areas of localized infection, in sepsis unless chemotherapy is being used concurrently, when total protein is less than 5.5 gm. per cent, and in circulatory disturbances without careful control of amount and rate of flow.

In hypodermoclysis, when a previous skin test for sensitivity to hyaluronidase is negative and when about 10 cc. of the fluid has flowed through each side, 500 viscosity units of hyaluronidase (previously dissolved in 1 cc. of distilled water) is injected into the lumen of the rubber tubing above the needles. The same area can now be used effectively for clysis over a period of three days, and will rapidly absorb 70 to 100 cc. of fluid per pound of body weight daily. With this enzyme the effectiveness of clysis is augmented by more than five times.

Passive immunization—Probably the most effective prophylactic agent developed in recent years against virus infections is gamma globulin. It is the most satisfactory substance available at present for the prevention and attenuation of measles[13] (Table 9).

In doses of about 0.1 cc. per pound of body weight, gamma globulin provides protection against infectious hepatitis, if given at least five days before onset of symptoms.

Recent mass experiments on the prevention of poliomyelitis seem to indicate that gamma globulin offers protection against this disease, either by prevention or by attenuation. Final evaluation should be completed during 1953 and 1954.

Gamma globulin prepared from general plasma pools is of little value in mumps. However, that from mumps convalescent serum, when given in doses of 20 cc., reduced the incidence of orchitis from 27.4 per cent to 7.8 per cent.[14]

There is some evidence[15] that large doses (20 to 60 cc.) of gamma globulin will cause rapid fading of the rash and striking amelioration of the toxic signs and symptoms of scarlet fever.

Epilepsy—TRIDIONE® (trimethadione) is said to be the first drug ever to be effective in petit mal epilepsy, and it will control about 1 of every 3 cases. It is toxic to bone marrow and therefore blood counts should be performed two weeks after treatment is initiated and monthly thereafter. If tridione is ineffective, paramethadione (PARADIONE®) may be tried in similar doses (Table 10). It is advisable to combine phenobarbital with these drugs since about half of the children with petit mal will eventually develop grand mal attacks.

Perlstein[16] describes a relatively new anticonvulsant, GEMONIL® (5,5-dimethyl 1-methyl barbituric acid), as unique among antiepileptic drugs because it is more effective in organic than in idiopathic epilepsy. Peterman[17] regards gemonil as second only to phenobarbital in control of grand mal seizures; moreover, it is effective without causing sedation.

Folic acid antagonists—A group of compounds have been synthesized which differ

TABLE 9

DOSAGE SCHEDULE FOR GAMMA GLOBULIN IN PREVENTION AND ATTENUATION OF MEASLES

AGE (Years)	ATTENUATION	PROTECTION
5 or less	0.25-1.0 cc.	2.0-4.0 cc.
6 to 10	1.5-2.0 cc.	5.0-6.0 cc.

TABLE 10

DOSAGE SCALE FOR TRIDIONE AND PARADIONE

AGE (Years)	DOSAGE (Daily*)
1-4	0.3-1.0 gm.
5-9	0.6-1.5 gm.
10 and older	1.0-2.0 gm.

*Divided into three doses (capsule or elixir) and administered after meals.

only slightly from folic acid, but which disturb cellular function and interfere with the normal metabolism of this substance. These folic acid antagonists (AMINOPTERIN®, a-methopterin, dichloro-aminopterin, etc.) are of great palliative value in acute leukemia of childhood, and will provide clinical and hematologic improvement and prolongation of life in about half of the cases treated. In treating acute childhood leukemia, 1 mg. of aminopterin may be given daily intramuscularly for two days, then 0.5 mg. daily orally until a remission in the bone marrow is observed. It is important to use the smallest dose that will induce a remission in order to avoid necrotic, ulcerating oral and gastrointestinal lesions and associated fatal hemorrhage.

Heavy metal poisoning—The discovery of BAL, British anti-lewisite (2,3-dimercaptopropanol) provided an effective antidote against arsenic, mercury and gold poisoning (Figure 2). The drug will produce toxic effects in doses of 5 mg. per kilogram of body weight in over half the patients treated. Usual doses of epinephrine (1:1000) will cause rapid improvement from toxic reactions, and 25 mg. of ephedrine sulfate 30 minutes prior to BAL administration will prevent toxicity.

The work of Warkany and Hubbard[19] offers evidence pointing to mercury poisoning (calomel-containing teething powder, worm pills, ammoniated mercury ointment, diaper rinses in mercury bichloride, etc.) as the cause of acrodynia, and indicates the effectiveness of BAL as an antidote in a dosage of 3 mg. per kilogram of body weight every four hours for two days, then every six hours for one day and finally every 12 hours for seven days.

It is important to emphasize that BAL should not be used indiscriminately in heavy metal poisoning in which its value is unproved. It not only has been found to be valueless in some cases, but moreover has actually augmented previously existing heavy metal toxicity. The value of BAL in lead poisoning is not well established. Agerty[20] states that sodium citrate, given orally in doses of 1 to 2 gm. three times daily for two to three months in children, appears to be the treatment of choice in plumbism. This implies, of course, a regimen including such supportive therapy as blood transfusions, parenteral magnesium sulfate, intravenous glucose and cranial decompression, if indicated. Recently EDTA[21] (ethylene-diamine-tetra-acetate) has shown such promise in preliminary studies that it may indeed come to occupy a most important place in treatment of lead poisoning.

Summary

A review of some of the newer drugs is presented with practical reference to clinical usefulness of these agents in diseases of infants and children. While the greatest advances have been made in the area of control of in-

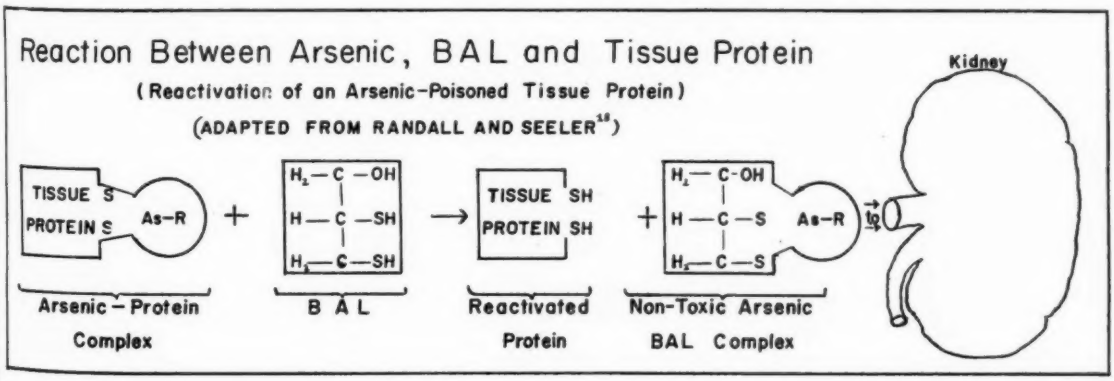

FIGURE 2

fection, the erratic nature of sickness in the growing young patient plus the overwhelming multiplicity of new and unfamiliar therapeutic agents impose a heavy burden on the physician in the selection of the appropriate drug combinations as well as the administration of optimal dosages with a minimum of adverse reaction. Along with many of the other newer drugs, the antihistaminics and the pituitary-adrenal hormones (ACTH and cortisone) are disappointingly weak as curative agents, but compensate largely through the symptomatic relief they afford.

REFERENCES

1. Alexander, Hattie: Advances in Pediatrics. New York, Interscience Publishers, Inc., 1952, vol. 5, pp. 19 and 22.
2. Ruegsegger, J. M.: Principles of sulfonamide and antibiotic therapy. New York J. Med. 51:222-224 (January 15) 1951.
3. Stollerman, G. H. and Rusoff, J. H.: Prophylaxis against group A streptococcal infections in rheumatic fever patients. J.A.M.A. 150:1571-1575 (December 20) 1952.
4. Price, W. C.: Sinobronchitis in infants and children. J. Pediat. 38:597, 1951.
5. Field, C. E.: Bronchiectasis in childhood. Pediatrics 4:355-372 (September) 1949.
6. A Medical Research Council Investigation. Brit. M. J. 2:1073, 1950.
7. Heck, W. E. and Hinshaw, H. C.: Clinical experience with a mixture of streptomycin and dihydrostreptomycin. Reported to the Veterans Administration (Army-Navy) Twelfth Conference on the Chemotherapy of Tuberculosis, Atlanta, Georgia, February 1953.
8. Lincoln, E. M. and Wilking, V. N.: Specific treatment of children with tuberculosis. Am. J. Dis. Child. 82:655-665 (December) 1951.
9. Stoesser, A. V.: Allergy in children and the antihistamines. J. Lancet 71:83-87 (March) 1951.
10. McQuarrie, Irvine, Ziegler, M. R., Wright, W. S., Bauer, E. G. and Ulstrom, R. A.: Further studies on the effects of ACTH on spontaneous hypoglycemosis. In: Proceedings of the Second Clinical ACTH Conference. New York, The Blakiston Company, 1951, vol. 2, pp. 69-79.
11. May, C. D., Stewart, C. T., Hamilton, Agnes and Salmon, R. J.: Infection as cause of folic acid deficiency and megaloblastic anemia. Am. J. Dis. Child. 84:728 (December) 1952.
12. May, C. D., Sundberg, R. D., Schaar, F., Lowe, C. U. and Salmon, R. J.: Experimental nutritional megaloblastic anemia. Am. J. Dis. Child. 82:282 (September) 1951.
13. Stokes, J., Jr., Maris, E. P. and Gellis, S. S.: Use of concentrated normal human serum gamma globulin (human immune serum globulin) in prophylaxis and treatment of measles. J. Clin. Investigation 23:531, 1944.
14. Gellis, S. S., McGuiness, A. C. and Peters, M.: Study on prevention of mumps orchitis by gamma globulin. Am. J. M. Sc. 210:661, 1945.
15. Weinstein, Louis and Potsubay, Samuel: A comparison of "symptomatic treatment," gamma globulin and penicillin in the treatment of scarlet fever. J. Pediat. 37:291-306 (September) 1950.
16. Perlstein, M. A.: Gemonil (5,5-diethyl 1-methyl barbituric acid); new drug for convulsive and related disorders. Pediatrics 5:448-451 (March) 1950.
17. Peterman, M. G.: Treatment of convulsions in childhood. Am. J. Dis. Child. 84:412 (October) 1952.
18. Randall, R. V. and Seeler, A. O.: BAL. New England J. Med. 239:1006 (December 23) 1948.
19. Warkany, Joseph and Hubbard, D. M.: Adverse mercurial reactions in form of acrodynia and related conditions. Am. J. Dis. Child. 81:335-373 (March) 1951.
20. Agerty, H. A.: Lead poisoning in children. M. Clin. North America 36:1592 (November) 1952.
21. Rubin, M.: Cited by Agerty: Paper presented at meeting of American Chemical Society, Milwaukee, Wisconsin, March 31, 1952.

Postgraduate Clinical NOTES

10. DISGUISING NAUSEOUS DRUGS

The poet Lucretius spoke of the art of covering the taste of nauseous drugs:

"As physicians use,
In giving children draughts of bitter juice,
To make them take it, tinge the cup with sweet,
To cheat the lip; this first they eager meet,
And then drink on, and take the bitter draught,
And so are harmlessly deceived, not caught;
For by this means they get their health, their ease,
Their vigor, strength, and baffle the disease."

Oppenheimer, Heinrich: Medical and Allied Topics in Latin Poetry. London, John Bale, Sons & Danielson, Ltd., 1928, p. 218.

GENERAL PRACTICE *Review*

This department offers the latest, proved methods for the treatment and management of commonly encountered conditions based on the extensive experience of the physicians who prepare these summaries for POSTGRADUATE MEDICINE.

The Hard of Hearing Patient

HOWARD P. HOUSE

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HOWARD P. HOUSE

ACCORDING to available statistics, approximately 1 out of every 10 persons has a hearing impairment. Modern methods of management have brought relief to many hard of hearing persons, and it is the purpose of this paper to acquaint the physician in general practice with these advances.

Types of Hearing Impairment

Impaired hearing is of three types: (1) conduction or middle ear loss, (2) perception or nerve loss and (3) otosclerosis, which is often a combination of both middle ear and nerve involvement. Impaired hearing due to malingering or hysteria is not a true pathologic entity and therefore will not be included in this discussion.

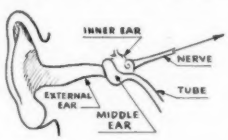

FIGURE 1.

Conduction (Middle Ear) Impairment

Etiology—Any pathologic condition that interferes with the transmission of sound vibrations to the inner ear (cochlea and auditory nerve) results in a conduction hearing loss. This interference may be present in the external ear canal, in the middle ear or in the eustachian tube. External ear canal obstruction is most commonly due to ceruminosis, furunculosis or foreign bodies. The function of the eardrum may be interfered with by perforation, edema or fibrosis (scars). Sound transmission through the middle ear may be impaired as a result of ossicular chain involvement such as dislocation, articular disease or necrosis, or of the presence of fluid, either serous or purulent, in the middle ear. Eustachian tube obstruction results in pressure changes within the middle ear and likewise interferes with sound transmission. Tubal obstruction may be due to altitude changes, inflammatory or allergic edema or adenoid hypertrophy.

Diagnosis—The diagnosis of conduction hearing loss is made on the basis of subjective and objective findings, tuning fork tests and audiograms.

The subjective findings in conduction loss are quite characteristic. The patient usually has a soft-spoken voice because external noise interference has been diminished and

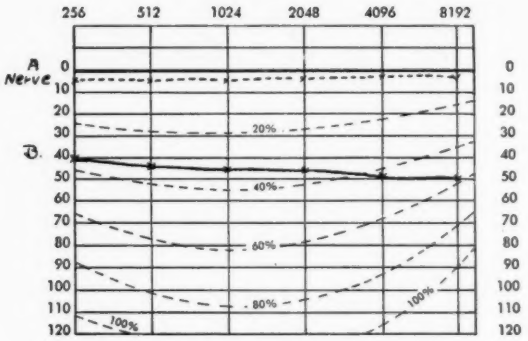

FIGURE 2. Conduction or middle ear impairment audiogram. A. Curve is the nerve response. B. Curve is the middle ear response.

he therefore hears his own voice loudly. The low tones are not heard well and therefore the patient will state that he hears better in a noisy environment, because other persons to whom he is talking are conscious of the noisy environment and speak with more intensity. Chewing of crunchy foods such as toast and celery sounds very loud to the individual with impaired conduction, and he often has to stop in order to hear table conversation.

Objective findings in conduction hearing loss may reveal structural and functional changes of the external ear canal, eardrum or eustachian tube. The sound of a vibrating 512 tuning fork placed in the center of the forehead of a person with conduction hearing loss will be referred to the ear with the greater impairment due to the exclusion of extrinsic sounds (Weber test). The sound of a vibrating 512 tuning fork no longer heard when the prongs are held an inch from the external ear will be heard when the shank is placed against the mastoid (Rinne test).

An audiometric reading will reveal loss of air-borne tones.

Treatment—Treatment of the patient with a conduction hearing loss depends on correction of the underlying pathologic condition or on furnishing adequate substitution.

Removal of any obstruction to the external ear canal is imperative. Cerumen is best removed by syringing, but this should be done only after the patient has assured the physician that he has had no previous ear disease. If a healed perforation exists, rupture may occur; if a perforation of the drum pre-existed, the irrigating solution may create or activate an otitis media. As with other foreign bodies, if the cerumen is firmly impacted or if previous ear disease has been present it is best to remove the cerumen by means of a small ear hook.

Correction of any abnormality of the eardrum, such as closure of an old perforation, is very desirable. This procedure is successful only in cases of dry, central perforation. It may be accomplished by freshening the edges with a caustic agent and placing some material such as paper or SCOTCH® tape over the opening, thus allowing epithelization to occur underneath. Marginal perforations, unfortunately, cannot be closed in this manner.

Conductive hearing impairment due to active middle ear disease necessitates every attempt to stop further destruction of the hearing mechanism. Acute otitis media must be treated early and adequately to prevent chronic infection. This is best accomplished by nasal shrinkage to evacuate the tube and by antibiotic therapy. If the eardrum is full or bulging, myringotomy should be performed routinely. If the fluid so encased in the middle ear is not drained, subsequent fibrosis will result both in further hearing loss and in subsequent attacks of otitis media. If the infection continues in spite of adequate treatment, an adenoidectomy should be performed at four weeks in a further attempt to ventilate and evacuate the eustachian tube. One or two attacks of acute otitis media justify an elective adenoidectomy. If the drainage continues for six weeks, it suggests bone necrosis in the mastoid cells. If a prophylactic, simple mastoidectomy is not done at this time, a chronic discharging ear may result, with permanent middle ear damage.

Artificial eardrums (Pohlman inserts) may be used in carefully selected cases of bilateral conduction hearing loss due to chronic ear disease with partial or total destruction of the eardrum and ossicles. A testing probe is used to determine the sensitive contact point on the medial wall of the middle ear. The insert of choice then is fitted to the ear canal so as to

contact this sensitive area. Artificial eardrums are of several types, such as the cotton pledget, the cellophane cone, molded rubber (Korogel) and the diaphragm rod.

All persons with conductive loss can hear with amplification made possible by the electric aid. When other means fail, the electric aid serves this type of patient very well. Its disadvantages, such as the cosmetic effect with the resulting psychologic manifestations, the battery nuisance and the telephone type of transmitted tone, are well known. One needs only to compare the hearing aid of today with its predecessors of 10 years ago to appreciate the marked advances being made in the electronic field. It is imperative that every person acquiring a hearing aid be adequately instructed in its use, for without such instruction the hearing aid often is relegated to a dresser drawer.

Altitude changes and upper respiratory infections frequently result in temporary obstruction of the eustachian tube due to edema or accumulated mucoid material. If the tube does not open spontaneously, an inflation or two usually will clear the lumen and restore hearing.

Allergic edema of the tube may result in a prolonged bilateral conduction impairment. In these cases there usually is an associated allergic rhinitis. The hearing difficulty may be relieved temporarily by inflation and by administration of ephedrine and antihistamines. After the diagnosis of an allergic tubal obstruction is established, a complete allergic study followed by the necessary desensitization is indicated in all cases.

Serous otitis media with fluid in the middle ear is often associated with an underlying allergy. Conduction impairment results and examination reveals a reddish pink discoloration over the lower half of the eardrum. A fluid level and air bubbles occasionally may be visualized through the drum. Treatment consists of myringotomy followed by inflation of the eustachian tube. Varying amounts of straw-colored fluid are expelled, following which there is immediate improvement in hearing. This treatment may have to be repeated and a complete allergic study made before permanent relief is obtained.

Lymphoid hypertrophy in the nasopharynx is the most frequent cause of conduction impairment in children. All such patients are entitled to a thorough adenoidectomy. If the hearing does not improve following surgery, adequate radiation therapy should be given to the nasopharyngeal area to eradicate further every vestige of lymphoid tissue about the eustachian tube orifice.

Perception (Nerve) Impairment

Etiology—Any pathologic condition which interferes with the function of the cochlea or the pathways of the auditory portion of the eighth nerve results in perception or nerve loss. These conditions include congenital malformations, allergy (edema of the cochlea), infection (labyrinthitis), acute and chronic systemic disease, drug sensitivities (alcohol, quinine, nicotine, streptomycin, etc.), nervous system disease (multiple sclerosis, syphilis, eighth nerve tumors), hemorrhage, acoustic trauma (blast injury), occupational deafness (prolonged exposure to high levels of noise), skull fractures which involve the temporal bone, and others. Arteriosclerotic changes in later life cause a common type of nerve impairment seen in older persons, known as presbycusis.

Diagnosis—Subjectively the patient with perceptive impairment, in contrast to the patient with conductive impairment, speaks

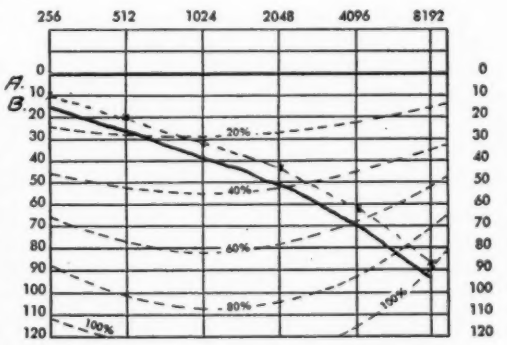

FIGURE 3. Perception or nerve loss audiogram. Note A and B curves are together, indicating no middle ear or conduction involvement.

loudly and in a monotone because he does not hear his own voice. Because he usually hears low tones better than high tones he is confused in attempting to converse in a noisy environment. Crunchy foods make no difference to this individual because he is unable to hear sounds from within or without.

Objectively the examination may fail to reveal evidence of ear disease. The sound of a vibrating 512 tuning fork placed in the center of the forehead is referred to the ear of lesser impairment, and will not be heard either when the prongs are held an inch from the external ear or when the shank is held in contact with the mastoid bone.

Audiometric readings will reveal loss of both air-borne and bone-borne tones of approximately the same degree. These findings are directly opposite to those encountered in the patient with conductive impairment.

Treatment—Unfortunately the medical and surgical treatment of perceptive hearing impairment is for the most part unsatisfactory. Once the nerve is damaged, the condition is permanent. Therefore treatment is directed not toward improving the individual's hearing but rather toward preventing further nerve loss. An excellent example of prevention is seen in the field of occupational hearing loss due to prolonged exposure to loud noise; control of noise at its source, adequate ear protectors and routine periodic audiograms should go far in preventing this type of perceptive impairment in persons working in high noise levels. A complete history and a thorough physical examination are indicated in all cases to eliminate every possible underlying cause. Use of massive doses of vitamin A, as well as thiamine chloride as advocated by some, in my experience has been of no value.

A hearing aid is of most benefit in cases of nerve impairment if the low tones and the high tones have deteriorated in about the same proportion. When the low tones have remained relatively good and the high tones are impaired, the use of a hearing aid becomes more difficult because of the amplification of the low tones. In marked nerve impairment, rehabilitation and auditory training with lip reading and speech conservation are essential. If the loss is congenital in origin, proper speech training must begin in the preschool age if the child is to be rehabilitated.

Otosclerosis

Etiology—The pathologic change in clinical otosclerosis consists of a developmental proliferation of the bone involving the area about the footplate of the stapes and the oval window which separates the middle ear from the inner ear. The exact cause of this proliferation is not known, other than that it is hereditary in nature.

Otosclerotic changes in the labyrinthine capsule have a very high incidence and are often found at autopsy in cases in which there had been no evidence of hearing impairment. How many persons go through life with otosclerosis which never manifests itself by involving the stapes footplate is not known.

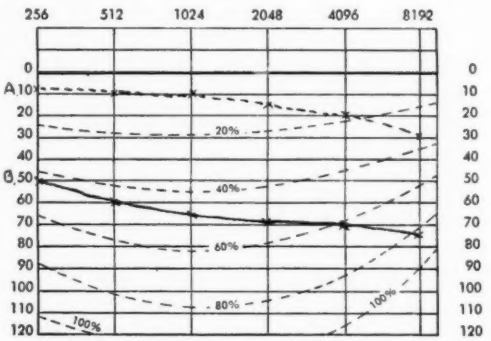

FIGURE 4. Otosclerosis. Note the mixed involvement of both the perceptive and conductive mechanisms.

Diagnosis—Otosclerosis is characterized by a progressive bilateral loss of hearing involving first the conductive and later the perceptive mechanism. It usually becomes apparent in early adult life and is frequently associated with tinnitus. There may or may not be a positive family history of hearing impairment. Frequently the patient has some reason for hearing loss, such as trauma, childhood disease or a recent upper respiratory infection. This unfortunately may cause the exam-

ining physician to err in the diagnosis of otosclerosis.

A thorough examination of the entire ear mechanism will fail to elicit any cause for the impairment. The eustachian tubes inflate readily, the eardrums appear thin and translucent, and no apparent pathologic condition can be noted.

By the time the patient seeks medical aid an audiogram will reveal a bilateral conduction loss of 25 to 50 decibels, with or without evidence of nerve involvement.

Any progressive bilateral hearing impairment occurring in early or middle adult life which on examination does not present evidence of ear disease suggests otosclerosis. This coupled with a coexistent tinnitus and a family history of impaired hearing without other apparent cause is almost diagnostic of otosclerosis.

Treatment—Perhaps no other group of persons has been subjected to more treatment without benefit than the unfortunate patients with otosclerosis. Repeated eustachian tube inflations, nose treatment, nose and throat surgery, eardrum massage, and various diets, endocrines, vitamins and minerals have all been put through their paces without noticeable benefit. When benefit has been derived, one is led to believe that the diagnosis of otosclerosis was in error, for it is difficult when one visualizes the underlying disease to understand how such therapy could have much reward.

The Fenestration Operation

Some 70 years ago a German otologist by the name of Kessel had a patient who was suffering from otosclerosis. The patient subsequently recovered his hearing in one ear following a skull fracture involving the temporal bone. Years later an autopsy revealed an open crack in the bone over the patient's membranous labyrinth. This finding led to a considerable amount of experimental work directed toward the surgical creation of an opening in the osseous labyrinth. It was noted that hearing often was restored as soon as this opening was made, providing the nerve function was capable of transmitting the sound to the brain. Likewise, as soon as the bony opening closed, hearing dropped back to its former level.

Passow, Kenkins, Barany, Holmgren and Sourdille are prominent names in the history of otosclerotic surgery and each made his contribution. Some 15 years ago Lempert developed the first satisfactory surgical technic which could be employed routinely in these cases. Since then he and others have modified the procedure until now the bony window made over the labyrinth remains permanently patent in all but 5 per cent of the cases in which the operation is performed. If the opening closes it will usually do so within the first six months after surgery and the hearing then regresses to the preoperative level.

As one may well realize, surgery of this type is very delicate and exacting. Fortunately the incidence of serious complications is very small. Today the patient with otosclerosis has two choices when his hearing loss becomes pronounced: (1) the hearing aid and (2) the fenestration operation.

The hearing aid will give satisfactory results in early otosclerosis, as in all cases of conductive impairment. Ultimately, if the otosclerotic process progresses, a hearing aid becomes increasingly difficult to wear and the patient must turn to rehabilitation and lip reading, just as in the case of advanced nerve impairment.

The fenestration operation is indicated in any case of otosclerosis in which the eardrum is intact and the nerve function is capable of transmitting the normal ranges of conversation to the brain. The degree of nerve function present is determined by tuning fork tests and audiometric readings. If these qualifications are present, the chances are 2 out of 3 that serviceable hearing can be permanently restored by the fenestration operation.

When one realizes that little or nothing could be done for these unfortunate persons a brief 15 years ago, this is indeed a tribute to otology.

The Physician's Responsibility

Hearing is indeed a priceless asset which

every physician is obliged to conserve. When a patient with a hearing loss seeks aid from the medical profession, the following course of procedure is advisable:

1. A complete personal and family history must be carefully and accurately obtained.

2. A thorough physical and otologic examination including complete hearing tests is essential.

3. After establishing the correct diagnosis and etiology, the entire problem should be carefully and fully explained to the patient and reassurance given that he will not become totally deaf. This is the chief concern of every person with a hearing loss.

4. The underlying cause should be eliminated when possible and medical and/or surgical treatment instituted *when indicated.*

5. If a hearing aid and rehabilitation measures such as lip reading and speech conservation are the procedures of choice, it is the physician's duty to direct the patient to the proper sources for this type of therapy.

6. The facts and prognosis should be completely explained in order to obtain full patient cooperation; this is essential if the person with a hearing loss is to get the most out of the future in spite of the existing handicap.

Conclusion

A brief summary of the problem of hearing impairment has been presented. It is the responsibility of the medical profession to recognize hearing impairment as a disease which handicaps approximately 10 per cent of the people in this country, and to institute every possible means available to be of service to these unfortunate persons.

Aplastic Anemia

TRUMAN G. SCHNABEL*

Philadelphia, Pennsylvania

IN the management of diseases of the blood and blood-forming organs, it is now generally appreciated that reasonably consistent satisfactory results can be achieved only by correlating carefully executed laboratory studies, historical revelations and physical findings. Spot diagnoses and random therapy may do well enough on occasions and only by chance, but even so the doctor must be left with a feeling of insecurity if he is not in the habit of classifying anemias morphologically and etiologically. He must feel particularly uneasy under these circumstances if such unselected treatment fails. So-called aplastic anemia is perhaps the most difficult to cope with even with the best of facilities for study and patient care, but many times more so when these are not available for the management of this anemia.

TRUMAN G. SCHNABEL

Anemia has long been designated as aplastic when study of the peripheral blood reveals a marked reduction in the number of leukocytes and platelets as well as erythrocytes; the bone marrow at the same time is unusually fatty and poor in hematopoietic elements.

Aplasia or hypoplasia of the bone marrow labels it more clearly than the term panhematocytopenia. A similar reduction of all cellular elements in the blood may also be a

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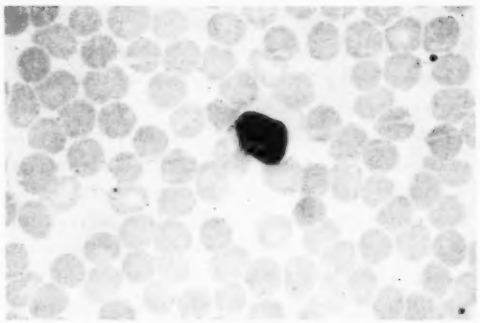
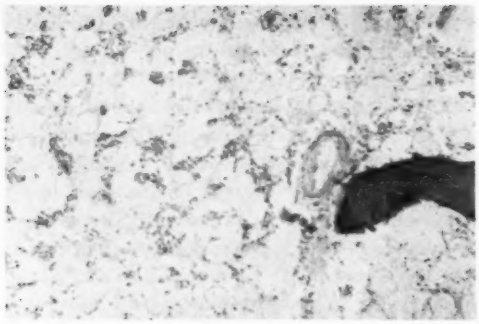


PERIPHERAL BLOOD, showing the anemia to be normocytic and normochromic in type. The few leukocytes present are lymphocytes.



VERTEBRAL BONE MARROW from a fatal case. Virtually all hematopoietic tissue is absent. The dark-staining cells in clumps are erythrocytes distending blood channels. Interstices between fat cells are edematous.

concomitant feature of leukopenic leukemia, a good many myelophthisic states, megaloblastic macrocytic anemias such as pernicious anemia, and various hypersplenic disorders including primary splenic panhematopenia.

Aplastic anemia is for the most part normocytic and normochromic with respect to the morphology of erythrocytes. On occasion it may be macrocytic, in which case the prognosis is more hopeful.

The red cells ordinarily show little or no poikilocytosis and virtually no anisocytosis. The bleeding time is markedly prolonged; the coagulation time is normal; the clot retracts little or not at all; the erythrocytic resistance to hypotonic saline solution is normal, and the tourniquet test is positive. Very few, if any, reticulocytes are to be found; there is no polychromatophilia or basophilic stippling, and no nucleated red cells appear in the peripheral blood. The leukopenia is of the granulocytopenic order, but may be lymphocytopenic as well. All of this indicates a fatty marrow with little hematopoietic possibility.

There appear in the literature descriptions of "aplastic anemia with hyperplastic bone marrow," a paradoxic situation which has been rather confusing. Such a condition could better be termed "aregenerative" or "refractory" anemia for the time being, because the notable feature is the lack of response to presently known therapeutic measures other than transfusions of blood. It is interesting that certain of these refractory states may develop following an initial marrow hypoplasia caused by protracted exposure to low concentrations of benzene or radiant energy. The marrow ultimately becomes hyperplastic and granulocytic leukemia occasionally occurs.

Aplastic anemia or any one of its variants is regarded as primary or idiopathic when the cause is obscure or indeterminable. When such anemias seem to be caused by the action of certain chemical and physical agents on bone marrow, directly or by reason of an acquired hypersensitivity, they are looked on as secondary in type.

Congenital hypoplastic anemia, an idiopathic variety, is discovered within some months after birth. The blood picture is not regenerative and is variably pancytopenic with no evidence of abnormal hemolysis. These infants may be maintained on blood transfusions until the bone marrow recovers, but more often they die of hemorrhage or some intercurrent infection.

The Fanconi syndrome is a special type of congenital aplastic anemia which frequently exhibits a familial tendency. Such patients are reported as having hypoplastic gonads, skin pigmentation and congenital deformations. They also present some degree of pancytopenia and dysfunctioning marrow, indicating that an inherited endogenous factor plays a role in the production of some varieties of aplastic anemia.

Acquired hypoplastic anemia, another idiopathic variety, is found for the most part in women during the third, fourth and fifth decades of life. In most cases these patients merely are tired, but often they are regarded as being either strictly psychoneurotic or lazy, depending on the I.Q. of the observer. Their anemia is normocytic and normochromic, and is accompanied by mild neutropenia and thrombocytopenia. Well studied and fortunately selected marrow shows a diminution of hemopoietic potential. Such women may undergo spontaneous remissions, but generally go on taking—of their own accord or by direction—all sorts of medicine which are of no benefit.

Idiopathic aplastic anemia is the best known primary variety of this disease. Patients suffering with this malady are for the most part young adults who present a waxen pallor and are usually febrile. The disease begins insidiously and almost uniformly progresses in a short time to a fatal issue.

The symptoms are based on the panhematocytopenia per se. From the anemia standpoint, such patients present various symptoms resulting from a decreased oxygen-carrying power of the blood; such symptoms involve the respiratory, cardiovascular, nervous, alimentary and genitourinary systems. The characteristic features of pernicious anemia in the nervous and digestive systems do not develop. Thrombocytopenia accounts for purpura and bleeding from the mouth and nose, in the eyegrounds and elsewhere. The leukopenia conditions ulcerative lesions in the mouth, throat and other parts of the body. There is no bony tenderness as is often noted in leukemia, and the spleen and liver are not enlarged. Regional lymph nodes may be tender and enlarged in the neighborhood of ulcerating lesions, the result of reactive hyperplasia.

The bone marrow is almost completely aplastic. Foci of red cell progenitors are more apt to persist than granulocytes or megakaryocytes. Reactive lymphocytosis may be so marked as to simulate lymphocytic leukemia, and plasmocytes and macrophages often are so numerous that the fundamental aplastic state is obscured. After multiple transfusions the bone marrow shows hemosiderosis, and in long-standing cases it may become extensively fibrotic. Some reports mention a relationship between hemochromatosis and aplastic anemia. More than likely these observations refer to an "exogenous hematochromatosis" following prolonged transfusion therapy.

Secondary aplastic anemia has been prominently identified with long-continued exposure to certain physical agents and a great number of different chemical substances. The clinical aspects do not differ sharply from those of the primary type. Chloramphenicol is currently being featured in this regard by published case reports of aplastic anemia associated with long-continued administration or interrupted use of this antibiotic. No other antibiotic except streptomycin is presently credited with a marrow-depressant effect. Of the anticonvulsant remedies, trimethadione (TRIDIONE®) and hydantoin (MESANTOIN®) occasionally may set up an aplastic anemia, and recently among the antihistamine preparations PYRIBENZAMINE® has been held accountable in aplastic anemia.

Mustard gas and the nitrogen mustards may effect a partial or complete inhibition of marrow, and according to some statistical studies gold compounds more frequently have the same effect. Cymene (sulfite pulp), ATABRINE®, dinitrophenol, trinitrotoluene, bismuth, mercury, silver, insecticides (VOLATITE®), hair dye, estradiol benzoate and some sulfonamides would also seem in isolated instances to have myelotoxic potentialities.

The toxic effect of benzol or benzene on the hematopoietic system has been a matter of observation and record for more than 50 years. Its varied action has been mentioned earlier. It is widely used in industry and continues to be an industrial hazard judging by reports in recent medical literature.

Organic arsenicals may result in a partial or complete hematocytopenia as part of an aplastic anemia, but no longer constitute much of a treatment hazard with the passing of the arsphenamines in the treatment of syphilis. Several reports, however, indicate that inorganic arsenicals also may produce a partial or complete hematocytopenia.

Ionizing radiation from various sources (roentgen and gamma rays, alpha and beta particles, protons and neutrons) may cause secondary aplastic anemia if the exposure is unusual in dosage and/or time. Of all the bodily tissues those which carry on hematopoiesis are the most sensitive to radiant energy, so that all sorts of marrow and hematologic responses may be forthcoming under varying circumstances of exposure and idiosyncrasy. Intermittent small doses continued for a long period of time may cause aplastic anemia. However, roentgenologists suffer from leukemia more frequently than does the rest of the population; thus it would seem that intermittent small doses delivered for many years may also have some sort of a stimulating effect on bone marrow as well as an inhibiting one. Continuous small doses may produce a macrocytic type of anemia with some variations, as exemplified and referred to previously in the celebrated case of a radium salt ingested by watch dial workers about 20 years ago. The alpha and beta particulate emanations from such a source have a shallow penetration potential. By contrast, however, recent studies have shown that gamma rays and neutrons liberated by atomic explosion reach the bone marrow in a short period of time.

Diagnosis

The treatment of aplastic anemia consists in the main of making the diagnosis. This may be somewhat difficult at times. It can be done straightway, but usually the procedure becomes one of exclusion. Aleukemic leukemia, multiple myeloma, osteoporosis, Hodgkin's disease, metastatic carcinoma and hypersplenic disorders must be ruled out when there is a pancytopenia. Purpura hemorrhagica, agranulocytic angina and pernicious anemia for the most part offer no great problem in differential diagnosis.

It goes without saying that all examinations must be thorough and complete. Nothing can be omitted. The history must reveal all the details of the patient's life, present and past, with special reference to occupation. Here one must keep in mind the hazards of industry, medication, cleansing materials, insecticides, depilatories, etc. The physical examination should likewise be most searching. Particular attention must be paid to the spleen, liver and superficial lymph nodes; they may be palpable in some patients with aplastic anemia but usually they are not enlarged.

Laboratory studies should include a counting of all cellular elements in the blood as well as a determination of its pigment content. In some institutions the request for a routine "C. B. C." does not bring forth platelet and reticulocyte counts, which procedure obviously is inconsistent. The possession of information from time to time concerning the morphology and number of erythrocytes, reticulocytes, leukocytes and platelets together with estimations of hemoglobin is exceedingly important in the management of this whole group of patients.

Other examinations should include those for the bleeding time, the coagulation time and that of clot retraction. Obviously, carefully done bone marrow studies—or, better still, such studies carried out in series—are a must in dealing with the whole group of anemias under consideration. Better results are obtained when the marrow is studied by sections of aspirated fragments than when dependence is placed on smears alone. Too often, dilute smears have been interpreted as indicating aplastic anemia in patients whose marrow is actually hyperplastic.

Biopsy of palpable lymph nodes is also indicated if there is any suspicion of the presence of leukopenic leukemia. X-ray studies of bones and the chest round out a minimum amount of patient study.

Treatment

After the diagnosis has been made, transfusions of fresh whole blood become the sustaining and chief treatment of aplastic anemia. They are the logical treatment as well, because the anemia is usually normocytic and normochromic. Bone marrow preparations, PENTNUCLEOTIDE®, folic acid, pyridoxine, liver extract, epinephrine and even iron are of no real benefit. Blood accurately typed, matched

and cautiously administered will supplement the existing erythrocytic, leukocytic and thrombocytic deficit.

The amount and frequency of transfusions should be governed by the degree of anemia, the presence of bleeding and ulcerative lesions together with the general physical status of the patient. The most important result to be attained is the prevention of bleeding; infection can in most cases be controlled by antibiotics. The life of transfused platelets in circulation lasts but a few days, while leukocytes disappear almost immediately after transfusion. It may be then that bleeding, ulceration and the numeric level of leukocytes and platelets will require daily transfusion therapy. The patient is apt to become actually plethoric, by reason of the much longer survival time of transfused erythrocytes, and it is sometimes necessary to withdraw 500 cc. of blood to make room for each fresh transfusion. The employment of coated plastic transfusion sets (Fenwal) preserves the donors' platelets and leukocytes better than standard sets, and as little time as possible should elapse between donation and administration of blood. Still more effective are direct transfusions, using a silicone-coated apparatus.

In due time the interval between transfusions may be prolonged as the marrow appears to recover, if such is to happen. The amount of each transfusion should be governed by varying circumstances, bearing in mind that 500 cc. of blood usually will improve the red cell status for adults by about 10 per cent in 24 hours. Much less blood will be required for children. Transfusions should be continued in appropriate amounts and frequency if only to relieve dyspnea and bleeding. Case reports from the English literature state that patients have been kept alive in this way for as long as nine years.

Transfusions are usually given by an intravenous route; veins must be carefully treated and preserved for repeated use. The superior sagittal sinus is available for the same purpose in infants with open fontanels. Sternal marrow and arteries are also available as emergency sites for blood transfusion. A lone report in 1948 from Sweden calls attention to the advantage in practicing marrow to marrow transfusion with the belief that normal marrow possesses some intrinsic hematopoietic factor which is lost in aplastic anemia. The efficacy of this technic will of course need some confirmation from other quarters.

Transfusion therapy of all types calls for a thoroughgoing knowledge of all matters pertaining to blood, including care and skill in its collection, preservation and administration. With all of this, various untoward transfusion reactions may occur and should be anticipated, e.g., subgroup incompatibilities may develop which ordinarily would not be troublesome in less often transfused individuals.

The continued exposure of patients with aplastic anemia to hazards which are deleterious to hematopoietic tissue must obviously be stopped.

The myelotoxic possibilities in drug administration must be weighed against therapeutic urgency. Patient idiosyncrasy or perhaps sensitivity to one drug need not be present with other drugs with marrow-depressant tendencies. Precautions concerning infections must be taken, and an adequate amount of rest must be the intent of written orders.

The iron content of the blood plasma in the disease under consideration usually is in excess of normal, as is also true of the free erythrocytic protoporphyrin. Under these circumstances it may be enough to prescribe a diet which is overbalanced in favor of proteins against carbohydrates and fats, and contains an adequate amount of vitamins, minerals and calories.

There may, however, be something gained in anticipation of bleeding, e.g., if hemoglobin-producing foods are well represented in the dietary prescription. Such foods, as Whipple and his collaborators suggested more than 20 years ago, include a list of animal organs headed by beef liver and kidneys and chicken gizzards, and a fairly large list of fruits and a few vegetables. The liver in aplastic anemia contains the antipernicious anemia principle and so no particular effort need be made to supply this principle either in food or parenterally. The usual methods calculated to improve the appetite of anorexic patients

are applicable in this disease and are usually needed.

Appropriate hemostatic procedures must be used locally when bleeding occurs in spite of transfusion therapy. Antibiotics are indicated when a low leukocyte level has conditioned ulcerative lesions and/or a serious infection. In this regard it must be remembered that chloramphenicol is now under grave suspicion as a marrow depressant.

Other antibiotics, however, such as AUREOMYCIN®, terramycin or penicillin should be used if the need arises and particularly if blameworthy micro-organisms exhibit a sensitivity to one or another of these agents. They should be administered orally and not parenterally so as to obviate the danger of creating new areas of infection. When parenteral administration seems imperative, large doses of long-acting preparations should be used with a view toward reducing the number of traumatizing injections. ACTH and cortisone apparently have favorable influence on the course of this disease only when the marrow depression seems to be on the basis of acquired hypersensitivity to some exogenous substance.

Splenectomy has a very dubious place in a therapeutic program for aplastic anemia. It has now been performed in a small number of patients suffering with this disorder. There has been no postoperative improvement observed in most cases, but a very few have shown a temporary remission; these were probably cases of panhypersplenism, misdiagnosed as cases of aplastic anemia by reason of panhematocytopenia and inadequate marrow study. If the spleen happens to be inhibiting hematopoiesis, then splenectomy would seem to be a gamble. On the other hand, if some extramedullary hemopoiesis is going on, as it rarely does even in small degree, then the operation becomes a most unfortunate bit of therapeutic practice. Such conditions would obtain only when the marrow is replaced (myelophthisis) and the extramedullary components of the reticuloendothelial system retain their blood-forming potentialities.

In industries in which aplastic anemia is a hazard, workers must be apprised of the nature of their occupation in this respect and must be educated and trained to protect themselves. Industry, on the other hand, must introduce facilities and devices which will control employee exposure.

When patients are receiving some medication having myelotoxic possibilities, particular attention must be paid to the report of new symptoms which may call for a discontinuance of treatment. Blood counts at the time of each treatment or at fixed intervals of time may also turn up evidence which will call for the termination of harmful medication. There is uncertainty as to the possible amount of prevention which the physician can bring about by careful patient and blood checking, but he cannot well afford to omit it when he is administering drugs which may depress bone marrow.

The author wishes to thank Dr. R. Philip Custer, Director of Laboratories, Presbyterian Hospital, Philadelphia, for his cooperation in the preparation of this review.

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Postgraduate Medicine

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AVIATION MEDICINE

THIS year marks the fiftieth anniversary of the first airplane flight and the one hundred and seventieth anniversary of the first balloon ascent. It is of special interest to us in the medical profession that it was a French apothecary, Pilatre de Rozier, who was the first man to fly and that only two years later a series of balloon ascents were made by Dr. John Jeffries, an American physician. The latter was not only the first American to fly but also the first to publish a book on aeronautics,[1] to do research on the composition of the upper air, to carry airmail and to make an aerial crossing of the English Channel. Thus from the very beginning there has been a great amount of medical interest in flying and the effects of flight on the human organism and this interest has grown steadily as aviation itself progressed.

Today there are over 4000 physicians in the United States alone who devote all or part of their time to the practice of aviation medicine to meet the needs of civil and military aviation. During 1952 the scheduled airlines of this country carried more than 27,000,000 passengers and it is estimated that by 1960 this number will reach approximately 40,000,000. Among the military services, the air component constitutes our first line of national defense and has as one of its functions the responsibility of evacuating sick and wounded military patients by air. To date, over 2,000,000 such patients have been transported.

In the future there will not only be a greater demand for physicians in the field of aviation medicine but their problems will be more complex than those with which they have had to deal heretofore. Experimental military aircraft are now operating at speeds and altitudes which are not made public for security reasons. Flight beyond the atmosphere and into space is being seriously discussed by both engineering and medical scientists.[2]

Commercial aviation is following in the footsteps of the military as far as aircraft performance is concerned. This means much higher speeds and higher altitudes which, combined with greater traffic density and other factors, pose serious medical considerations. Great Britain is even now operating commercial jet transports at a cruising speed of 480 miles per hour which is far in excess of the world's aircraft speed record set in 1935. The British have under construction a later model of this commercial transport which will cruise at 600 miles per hour.

A few years ago the postgraduate courses of instruction in aviation medicine averaged 12 weeks in length. However, the knowledge required to become competent in this field has expanded with such rapidity and has become so complex that a training program covering a full six years has been established.

After internship, at least two academic years of graduate study must be successfully completed in a school accredited for the purpose by the Council on Medical Education

and Hospitals of the American Medical Association. This is followed by a residency of at least two years in aviation medicine including planned instruction, observation and active participation in an organized aviation medical training program. One year of this residency may be an approved clinical residency in a field directly related to aviation medicine. In addition to the above, there must be an additional two years of practice under proper supervision before an individual becomes eligible to take the examination for board certification. A final requirement is that the individual participate frequently and regularly in aerial flight in order that he may be thoroughly familiar with the medical problems resulting from the aerial environment and from aircraft performance.

In 1949 the Aero Medical Association appointed an Interim Board of Aviation Medicine with the view to obtaining recognition of aviation medicine as a specialty and board certification for those who were qualified. On the advice of the Advisory Board for Medical Specialists, affiliation with the American Board of Preventive Medicine was sought and successfully accomplished. At its annual meeting in Chicago in February 1953, the Council on Medical Education and Hospitals of the American Medical Association, on the recommendation of the Advisory Board, granted authority to the Board of Preventive Medicine to certify qualified candidates in aviation medicine as well as in public health. This recognition by organized medicine inaugurates a new era in aviation medicine in the United States and offers an opportunity for recognition to its many practitioners who have contributed much more than is generally realized to the progress and safety of aeronautics and hence to our commerce and to our national defense.

HARRY G. ARMSTRONG
Major General, USAF (MC)
Surgeon General

1. Jeffries, J.: A Narrative of the Two Aerial Voyages of Doctor Jeffries with Mons. Blanchard; with Meteorological Observations and Remarks. London, J. Robson, 1786.
2. White, C. S. and Benson, O. O. (Editors): Physics and Medicine of the Upper Atmosphere: A Study of the Aeropause. Albuquerque, The University of New Mexico Press, 1952.

HOUSEHOLD DETERGENTS

Household detergents rapidly are increasing in use both in this country and abroad. Recently Dr. Geoffrey Hodgson[1] of the Welsh National School of Medicine has noted some of the dangers and compared the advantages of detergents over soap. Thus the new detergents have the advantage over soap of not being inactivated by the hardness of water. They are active in alkaline, acid and neutral solutions. Solids are left suspended in the detergent solution and are not redeposited on fabrics during washing.

Formerly many women were sensitive to excessive contact with soaps but more recently our soaps are being prepared with greater care. Hodgson points out that in a washing solution, a concentration of detergent of 1 per cent is used as opposed to 5 or 6 per cent in a soap solution. The detergents may be sold in liquid form or as a packet containing a powder. Sometimes the detergents are reinforced with phosphates. The new detergents and soaps remove both dirt and grease rapidly. Certain skins, however, particularly those of old people, are damaged by irritations and have poor resistance to chemicals. People who soak too long in a very hot bath may also respond badly to soaps and detergents. Some of the problem comes from the removal of fats from the skin. More time must elapse before the exact incidence of irritation and discomfort can be determined. However, the skin may be protected by the application of creams and lotions which are now widely distributed and, of course, by the wearing of protective gloves.

In a comment on this article, the London *Lancet*[2] came forth with a little note that aroused excitement all over America since they blame the flying saucers on the use of detergents. Here is what they say exactly in their editorial.

When the detergent leaves the kitchen sink, other problems arise. At the sewage works it is usual, especially on Tuesdays, to find that the agitation in the aeration tanks has produced a surface layer of foam as much as six feet deep. The narrow service "roads" between the tanks

are slippery and dangerous; and huge masses of foam are liable to be whipped off by the wind, perhaps carrying pathogens and certainly a potential danger to car drivers, on whose windscreens they may alight. In America such masses of foam are believed to have accounted for some "flying saucers."

The *Lancet* is also disturbed to some extent about the possible effects of the detergents on fish if the detergents happen to reach rivers and streams in the processes of sewage disposal. Their only answer to the problems that arise is more research.

MORRIS FISHBEIN

1. Hodgson, Geoffrey: The use of household detergents and their dangers. Practitioner 170:166 (February) 1953.
2. Detergents. Lancet, February 21, 1953, p. 383.

ATOMIC MEDICINE

Continuing experiments and clinical experience in the field of atomic medicine indicate a gradually widening field of usefulness for radioactive isotopes therapeutically as well as increased usefulness of those that have been applied in diagnosis and research.

Iodine 131 has been employed therapeutically for 15 years, a sufficient length of time to evaluate some aspects but not to answer clearly the question of its potential carcinogenicity. Among the several thousand patients already treated, no instances of radiation-induced carcinoma have developed. In general a conservative approach is still being followed, and it is felt best to restrict its use primarily to cases of thyroid cancer and to inoperable cases of hyperthyroidism or those not satisfactorily responding to operative treatment. From the diagnostic standpoint, radioiodine is of unusual value in determining the level of thyroid activity and in localization of functioning thyroid cancer metastases. Combined with fluorescein, it is of value in the localization of brain tumors. Combined with protein (as iodo-albumin, for example), the isotope has brought great advances in understanding and localizing antigen-antibody reactions.

Gold 198 is being used increasingly for the control of disseminated cancer involving serous cavities. While in no sense a cure, it has much palliative value and has been used effectively, particularly for the control of formation of excess fluid in cases of carcinomatosis peritonei and hydrothorax due to metastatic tumor. Its effect seems to be not only on the tumor cells but also to some extent on the secretory activity of the mesothelial cells as well. The radioisotope is instilled in colloidal form into the cavity to be treated.

Phosphorus 32 has proved of value in therapy of polycythemia vera, and is sometimes of value in retarding the progress of leukemia and of plasma cell myeloma. In the latter two, however, it is not the treatment of choice and is best employed only if other methods have failed.

External radiation by radiocobalt and the use of radiocobalt for implantation purposes have been increasing. While a useful addition to the physical agents available for cancer therapy, its chief value is in its relatively low cost rather than in any special virtue inherent in its particular type of radiation, which is quite similar to the more penetrating gamma rays of radium. Very powerful sources of radiation can be obtained running up to 1000 curies but these are of necessity relatively limited as to the number that can be established. The Atomic Energy Commission has been active in advancing the field in this country; several installations for cobalt therapy exist in Canada.

A new technic arresting in concept and justified because of the inherent danger only in rather desperate situations is the technic evolved by the Brookhaven National Laboratory of the Atomic Energy Commission and Dr. William H. Sweet for the therapy of surgically inaccessible or highly malignant brain tumors. The technic is to make use of the selective uptake by the brain tumor of boron ions and then to irradiate the appropriate portion of the head of the patient with a flux of neutrons from the atomic pile. These neutrons captured by the boron ions lead to the emission of a highly ionizing and poorly penetrating alpha particle, thus giving selective radiation within the substance of the

tumor. This technic is still too new to be evaluated but may hold some promise, not only in this particular field but also may be applicable to the therapy of certain other inaccessible tumors as well.

SHIELDS WARREN

THE EXACT USE OF MEDICAL TERMS

THE most recent edition of the Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death, adopted in 1948 by the World Health Organization, begins with the statement that classification is fundamental to the quantitative study of any phenomenon. Statistical classification is often confused with nomenclature. A medical nomenclature is a list of approved terms for describing and recording clinical and pathologic observations. In either of these procedures, however, the terms selected must be used with great exactitude.

Sometimes advances in medical knowledge make difficult the use of certain terms because new facts change our concept of the conditions described by the terms mentioned. For instance, a person may take a large dose of a drug of the type of atropine or strychnine and as a result be poisoned by the drug. He may ingest a small, often an infinitesimal, amount of another drug and as a result have urticaria. Urticaria or an eruption of any kind associated with such special reactivity to certain drugs is in many books described as poisoning. Indeed our knowledge of the mechanisms involved in allergies may not yet be sufficient to make possible an exactness in describing what occurs sufficient for hospital records which largely follow the Standard Nomenclature of Diseases and Operations. Many conditions, from the point of view of the pathologist, are not certainly determinable even after postmortem examination.

The International List of Causes of Death, for another example, puts poisoning due to mushrooms, to plants used as food, and to shellfish under one classification and then carefully says that the title excludes *Salmonella* food poisoning, staphylococcal food poisoning, botulism and food poisoning due to hypersensitivity. The same classification assigns a special number to hay fever, asthma, angioneurotic edema, urticaria, and allergic eczema and lists under another number entitled "Other Allergic Disorders" allergy without any of these manifestations, allergy to cosmetics, dandruff, drugs, dust, feathers and food, and then excludes allergic purpura, anaphylactic shock and serum sickness. This classification must have given the board great concern; obviously even a greater burden comes to the physician working in a hospital who tries to make the distinction in classifying his cases for the hospital records.

The dictionaries are not exact in this matter. An excellent dictionary states that allergy is an altered reaction capacity to a specific substance which will cause no symptoms of hypersensitivity in the nonsensitive. This dictionary presents four types of allergic diseases, including (1) anaphylaxis, (2) atopic diseases which depend on an inherited constitutional capacity and which include hay fever, vasomotor rhinitis, asthma, urticaria, drug sensitivity, etc., (3) serum sickness and (4) contact dermatitis. One way to avoid these difficulties would be to employ other words, such as the word *capacity* (used in the third definition for allergy) which the dictionary defines as the power of receiving, containing, holding or absorbing, or such a word as *reactivity* which is simply the capacity of the body to react to a certain substance or possibly *susceptibility* which is the opposite of immunity. The word susceptible is defined as sensitive to an impression or influence.

Another dictionary defines allergy as a condition of unusual or exaggerated specific susceptibility to a substance which is harmless in similar amounts for the majority of members of the same species. This term embraces all types of human hypersensitiveness. Obviously under this definition the concept of poisoning does not enter in, at least not poisoning to the point of producing death.

The whole question is rendered especially serious in relationship to the reactions of the human body to many of the new drugs and

similarly to the old drugs. A person who has a mild rash following the taking of a laxative such as phenolphthalein or cascara is perhaps not poisoned; he may be susceptible but he need not necessarily be allergic. With the drugs which may produce purpura, nerve disorders or blood dyscrasias, such as antibiotics, antihistamines or antispasmodics, again the question is whether or not this is allergy, poisoning, susceptibility or simply toxicity.

MORRIS FISHBEIN

ASTHMA IN CHILDHOOD

In his thought-stimulating article on allergy, and other stress-conditioned illness, Dr. Richard Harper[1] proposes the thesis that a significant part is played in allergic illness by vestigial nervous defense paths which are now of little or no importance in the normal physiology of man though they become available in times of stress. As an example he takes the problem of asthmatic and allergic children. A majority of these children boarded in a school in which everything is done to maintain a wholesome, large family emphasis without fuss or strain. Everything possible is done to encourage an atmosphere in which good health is regarded as natural and normal and any illness is something which will be short and respond to treatment. This attitude is carried into the sickroom and care is taken to see that the neurotic or allergic child who becomes ill is allowed to realize that he will soon be well enough to get up and that then life will be much more interesting than it is in bed. For this reason the special requirement is that children are not entertained in bed; they are given only a minimum of books and occupations but they are told of all of the wonderful fun that the other children are having out of doors. This has been found an important factor in nursing the child who has been encouraged to regard himself as delicate and who has reached the stage where he often prefers life in bed.

During recent years a small proportion of severely allergic children have come to this school, frequently arriving with special bedding, sprays, nose drops, ear drops and regulations as to climate and diet. Often a large batch of prescriptions from medical authorities on allergy accompanies the child. The school has adopted the practice of ceasing to use all drugs and ending the limitations on activities immediately on the child's arrival. The school authorities find that the child settles down easily and soon loses his asthmatic or other allergic manifestations. The threshold at which an attack can be produced is raised to a significant degree. In addition the turgescence of the mucous membranes of the nose rapidly subsides, the obstruction of drainage of sinuses is removed, and sinus infections seem to clear promptly. The self-confidence of the child increases when he finds he can eat and play without having an attack.

Observations have shown that the arrival of a parent or relative promptly brings on an attack and examples of this are cited. In his stimulating article, Dr. Harper notes that this school can only supply a feeling of security and absence of fear and stress. It does not provide drugs or fussy nurses, but simply a lot of healthy, normal young companions and a sane and confident attitude toward illness and accident.

The clinical examples quoted, according to Dr. Harper, demonstrate the remarkable extent to which psychologically conditioned mechanisms alter both the severity of stress-conditioned illness and the threshold at which its diverse manifestations can be produced. In the United States this situation has been seen repeatedly when parents carry asthmatic children long distances and put them under different conditions of life for a time while they are receiving various treatments. The children promptly develop a different threshold of excitation and are pronounced cured but often relapse the moment they return home.

MORRIS FISHBEIN

1. Harper, Richard: Allergy, and other stress-conditioned illness: a suggested association with obsolete autonomic defence reflexes. Brit. M. J., p. 392 (February 14) 1953.

The Antiquity of Disease

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ALTHOUGH disease is several millions of years old, geologically speaking, it is of very recent origin. The fossils of animals and plants found in the earliest strata of the earth's crust show no recognizable evidence of disease, although bacteria of a nonpathogenic type had appeared. However, in the early Paleozoic stratum, some 30 millions of years ago, there is indubitable evidence of osteoarthritis, fractures and bone tumors in reptiles and fish. A dinosaur excavated in Wyoming revealed an hemangioma of the vertebral canal. The fossils of the tsetse fly unearthed in Colorado suggest that a disease similar to trypanosomiasis was prevalent over this part of the earth and probably was responsible for the extinction of certain mammals. Osteoarthritis and osteosarcoma were common in cave bears, and accinomycosis appeared in Miocene horses.

Nor was earliest man spared from disease. In 1891 Dubois, a Dutch army surgeon, was digging in the basin of the Solo River of central Java when his eyes fell upon the teeth of a peculiar kind of ape. He dug fervently a few feet from this spot and there lay the bones of Pleistocene man *(Pithecanthropus erectus)*, 500,000 years old. Just as it was a coincidence that the first written work of man was a medical treatise (The Edwin Smith Surgical Papyrus), so too, the first man discovered showed a pathologic phenomenon, a severe osteoarthritis of the femur. Furthermore, the Heidelberg man was found to have had Pott's disease of the spine. Neanderthal man disclosed osteomyelitis of the left humerus and rickets of the left ulna, and Piltdown man loomed large with acromegaly. Paintings visible to this day on the walls of caves visited by the massive-brained Cro-Magnon man of 20,000 years ago give clear evidence of endocrinal obesity, such as portrayed by the Venus of Willendorf.

By the time historical man appeared on the earth, disease was identical with that endured by twentieth century man. Thanks to the burial customs and the hot, arid climate of Egypt, the 30,000 splendidly preserved mummies studied by Elliott Smith, Wood Jones and Sir Marc Ruffer display alveolar periostitis, prolapse of the rectum, pericecal adhesions (healed appendicitis), gallstones, cirrhosis of the liver, arteriosclerosis, pneumonia (with exudate in the alveoli containing diplococci), anthracosis of the lungs, abscess of the kidneys, *Bilharzia* or *Schistosoma* eggs in the kidneys, urinary bladder stones, rickets, poliomyelitis, club foot, genu valgum, achondroplastic dwarfism, kyphosis, osteosarcoma, Pott's disease and lesions suggestive of smallpox. Breasted reports having found carcinoma of the breast. Ramses II had acne vulgaris. The dystrophia adiposa genitalis that affected the youthful heretic king Ikhnaton, whose dominions comprised in 1375 B.C. the whole of the then civilized world, led to physical

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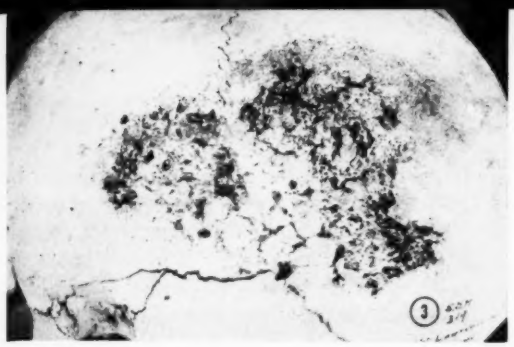
indolence and, in turn, to the collapse of his empire. Of course fractures were commonplace. How King Sekenenre died in 1870 B.C. was never known, but excavation at Der El Bahri in 1880 A.D. demonstrated that he was struck in the skull with an axe and a spear as he lay on his right side, probably in combat with the Hyksos, barbarians of Asia.

Ancient Peruvian pottery depicts uta or dermal leishmaniasis (kala-azar or Dumdum fever), and goundou or nasal yaws. Verruga peruana mystified the ancient doctor of Peru until Daniel Carrion, a medical student in Lima, Peru, inoculated himself in 1885 with blood from a verruga nodule. His unfortunate death one month later from Oroya fever emphasized the identity of the two diseases, a fact confirmed by Noguchi in 1926. Amongst the pre-Columbian Indians, osteoarthritis, so well emphasized by Ales Hrdlichka and Eric Stone, was common, and to a lesser degree Pott's disease also was present. Lues may or may not have existed.

Rational medicine has developed from several hundreds of thousands of years of probing, testing, analyzing, comparing, speculating, groping, fumbling and erring. We live because untold thousands have died. We have learned from the mistakes of both the countless host who had suffered and those who had cared for the suffering. No one has stated the determination of man to rid himself of illness better than Oliver Wendell Holmes in his valedictory address in 1871: "There is nothing man will not do. There is nothing they have not done to recover their health and save their lives. They have submitted to be half drowned in water and half choked with gasses, to be buried up to their chin in earth, to be seared with hot irons like galley slaves, to be crimped with knives like cod fish, to have needles thrust into their flesh, and bonfires kindled on their skin, to swallow all sorts of abominations, and to pay for all this as if to be singed and scalded were a costly privilege, as if blisters were a blessing and leeches were a luxury. What more can be asked to prove their honesty and sincerity?"

Who will say how much of our present-



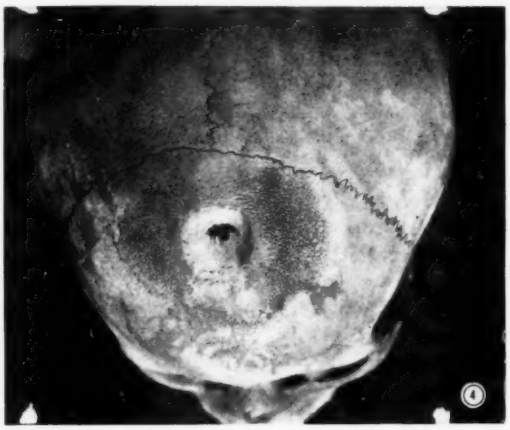


FIGURE 1. X-ray of unwrapped Egyptian mummy showing scoliosis of the thoracic spine.

FIGURE 2. Hypertrophic osteoarthritis with fusion of vertebrae, or poker spine. Eskimo—St. Lawrence Island, Alaska.

FIGURE 3. Syphilitic osteitis of the skull in an Eskimo of prehistoric days.

FIGURE 4. Osteoporosis of skull—prehistoric.

FIGURE 5. X-rays of two unwrapped Egyptian mummies, showing hydrocephaly.

(Photographs courtesy of the Chicago Museum of Natural History.)

day medicine stems from the nebulous past? Certainly many medicaments we use daily have done so—stomachics, carminatives, antispasmodics, emetics, purgatives, vermifuges, lachrimatory and sternutatory agents, cough sedatives, styptics, diuretics, aphrodisiacs, hypnotics, anesthetics, vesicants, rubefacients, decoctions and embrocations. And how ancient are the procedures of blood-letting, enemas, lavage of the various body cavities, cupping, needling and leeching. From the Melanesians we learn massage; from the ancient Hindus, the recently-used hypnosis; from the Chinese, vaccination against smallpox; from the ancient peoples of the Near East, immunization against snake bite, and from the American Indians, a sound, healthy body. Salicin for rheumatism, ipecac for diarrhea, hashish and henbane for pain, curare (ancient poison used on arrow tips) for relaxing muscles: all specifics—and ageless! The Countess of Chinchona is supposed to have been cured of malaria because of the advice of natives of South America that she should take Peruvian bark. It was hailed as a panacea upon its intro-

duction by the Jesuits into Europe in 1632.

The ancient doctor rejoiced in his surgery and attained a remarkable degree of dexterity. Most skillful was he in a procedure which in recent centuries had been a dreaded, formidable operation, and which more recently has been made commonplace by Victor Horsley and Harvey Cushing's method of trephining the skull. Without knowledge of anesthesia as learned by modern men from Crawford Long and Horace Wells and without benefits of Lister's antisepsis, the ancient doctor carved one or two holes in the vertex of the skull for causes little different from those existing today: for relief of epilepsy, insanity, severe headache, blindness and depressed skull fractures. The bone chipped away was used as amulets—prophylactic agents to ward off future disease. Some 500 skulls obtained from Peru, France and other parts attest to this operation. Many patients survived, thanks to the inherent powers of resistance of early man.

The operations now done on the sexual organs are equally embedded in the nameless past; circumcision, clitoridectomy, infibulation, castration, and mica or external urethrotomy (to prevent insemination).

The sincipital "T" operation and amputation of fingers were probably ritualistic. Drainage of abscesses, removal of foreign bodies, and suturing of wounds with thorns and animal hair or ants' pincers were commonplace. Fractures, exceedingly common among the pyramid builders, were corrected for the most part with fairly good results.

What is disease, asks ancient man, and how and why does it afflict us with pain and shorten our lives? He sees a relationship between cause and effect in the case of violence—injury due to a rolling boulder, illness due to the ingestion of a poisonous plant, or death due to a spear thrust; but in the case of fever, tumor, or inanition he sees only effect. The cause belongs to the realm of the mysterious, the obscure, the unknowable, the occult, the mystic, the terror-stricken. Perhaps the heavenly bodies—the stars, the moon, the sun—or the gods residing there are displeased and punish man with pestilence and disease, as well as with war, crop failure, floods or lack of rain. If so, they must be placated and assuaged by gifts, sacrifices and prayer. Demons living unhappily in woods, trees or rivers, in certain animals as serpents and crows, in dead human bodies, or in living men of his own or another tribe pounce upon the unwary victim and extinguish his life. To crush this evil, the strongest, most intelligent and crafty man of the tribe, schooled in the secrets of nature—the witch doctor—through conjuration, exorcism, threat or magic, through dancing and violent shrieking, through the use of time-honored rituals as the wearing of hideous masks and flaming red cloaks, or waving about a lizard's tail, will drive the demon away. To cite an extreme example of irrational medicine, the stomachs of infant Egyptian mummies have contained a skinned mouse, given as a drug to a dying child. Backward people of modern Scotland have administered an infusion of mouse for severe whooping cough.

To us, blessed by hundreds of centuries of medical knowledge gleaned from empiricism and experiment, this sounds diverting if not senseless. But let us never forget that ancient medicine is bound intimately with magic, philosophy and religion. Religion has nursed medicine through its most trying period and continues to play a not unimportant role to this day. Only until recently philosophy was an integral part of the medical education. And magic and superstition manifest themselves most strongly in quack and folk medicine, which dictate the principles upon which is based the therapy of a large segment of the world's population today.

The contributions of ancient medicine to modern medicine are so vast that, with Neuburger, we of today can extend our hand across the abyss of centuries and say to the ancient doctor, "Thank you for building the rock upon which we stand," and together we can stretch our arms skyward when our patient's life is snatched away, and say, "Whatever power or guidance there be in this Universe, give us strength of mind to learn why demons and bacteria, why malicious gods and tumors, why witches and metabolic demons, why black magic and vascular lesions take away our loved one!"

Index to Volume 13
Subjects

ABDOMEN, acute disease in, 19
Abortion and hemorrhage, 119
Accidents, and environment, 201; prevention in industry, 328
Acne, treatment with vitamins, A-34 (Mar.)
ACTH, *see* Cortisone
Adrenals, abnormalities of surgical significance, 500; effect in allergy, 383
Alcoholism, nutritional research and, 306; treatment with antabuse, incidence of suicide and, A-26 (Apr.)
Allergy, adrenals in, 383; bedbug bites as cause of asthma, A-28 (Apr.); dermatitis, atopic (infantile eczema), 252; fallacies in diagnosis and treatment, 410; food sensitivity as cause of dermatitis of hands, 26; milk, use of meat in, 461; treatment with antihistamines, 266
Ambulation, early, effects of, 206
Aminophylline, tolerance to oral administration, new approach to, 432
Anemia, aplastic, 568; sickle cell, 224
Antabuse and suicide, A-26 (Apr.)
Antibiotics, *see also* Penicillin; indications in childhood, 552; treatment of streptococcal infections in children, 153; treatment of tuberculosis, 519
Antihistamines, indications in childhood, 557; treatment of allergic diseases, 266
Appendicitis as cause of acute abdominal pain, 19
Arderne, John, father of English surgery, 479
Arthritis, osteoarthritis of hip, surgery for, 495
Asthma, and allergy to bedbug bites, A-28 (Apr.); cardiac, differentiated from true bronchial asthma, 89; bronchial, treatment with cortisone, 389
Atherosclerosis, nutritional research and, 305

BAL (2,3-mercaptopropanol) treatment of heavy metal poisoning in children, 561
Bedbug bites as cause of asthma, A-28 (Apr.)
Biological Photographic Association exhibit, 443
Biostatistics, 334
Bladder papilloma, 423
Blindness, prevention of blindness due to glaucoma, 2
Blood, donors, selection, A-30 (May); dyscrasias, *see also* Anemia; dyscrasias and bleeding gums, 100; dyscrasias due to drugs, 185; dyscrasias, splenectomy for, 507; methemoglobinemia in infants given polluted water, 293; pressure, high, due to adrenal tumor, 504; pressure, high, retinal arteriolar signs of, 239; pressure, high, sympathectomy in infants and children, 68; transfusion in gastrointestinal hemorrhage, 161; vessels, *see* Atherosclerosis; Varicose veins
Bone, *see also* Fractures; growth disturbance due to fractures of distal epiphysial cartilage of radius, 39; marrow, influence of drugs on, 185; tumors, eosinophilic granuloma, 229
Book reviews, Advances in internal medicine (Dock), A-60 (June); Bacterial and mycotic infections of man (Dubos), A-54 (June); Biochemistry of disease (Bodansky & Bodansky), A-56 (June); Cardiac therapy (Stewart), A-58 (Jan.); Congenital anomalies of the heart and great vessels (Schnitker), A-50 (Mar.); Cornell conferences on therapy (Gold), A-58 (Mar.); Culdoscopy (Decker), A-60 (Jan.); Diagnostic and experimental methods in tuberculosis (Willis), A-56 (Mar.); Diseases of the heart and arteries (Herrmann), A-58 (June); Disorders of the circulatory system (Craig), A-52 (Apr.); Electrocardiography in practice (Graybiel, White, Wheeler and Williams), A-54 (June); The esophagus and its diseases (Palmer), A-62 (Jan.); Essentials of infant feeding for physicians (Meyer), A-54 (Apr.); Gastrointestinal x-ray diagnosis (Ritvo), A-56 (Mar.); Gynecological and obstetrical pathology (Herbut), A-54 (June); Handbook of fracture treatment (Compere, Banks and Compere), A-54 (Feb.); An introduction to medical science (Boyd), A-60 (Jan.); The knee and related structures (Lewin), A-64 (Jan.); Manual of gynecology (Taylor), A-54 (Feb.); Metabolic bone disease (Snapper), A-62 (Jan.); Neurosurgery in general practice (ver Brugghen), A-54 (May); 1951 year book of physical medicine and rehabilitation, A-64 (Jan.); 1953 medical progress (Fishbein), A-54 (May); 1952 year book of drug therapy (Beckman), A-58 (June); 1952 year book of general surgery (Graham), A-52 (Apr.); 1952 year book of medicine, A-60 (Jan.); The 1952 year book of obstetrics and gynecology (Greenhill), A-50 (Apr.); The 1952 year book of pediatrics (Gellis), A-56 (May); Office psychiatry (Moench), A-58 (Mar.); Pediatrics in general practice (Hughes), A-58 (Mar.); Pheochromocytoma and the general practitioner (DeCourcy), A-56 (May); Physiological bases of gynecology and obstetrics (Reynolds), A-56 (June); Practical dermatology for medical students and general practitioners (Lewis), A-50 (Apr.); The principles and methods of physical diagnosis (Leopold), A-54 (Mar.); Progress in fundamental medicine (McManus), A-52 (Mar.); Psychiatry and medicine (Osborne) A-52 (Feb.); Rheumatic fever (Symposium), A-50 (Feb.); Sterility: its cause and its treatment (Rommer), A-52 (Apr.); Surgery of the chest (Johnson), A-54 (Mar.); Synopsis of pathology (Anderson), A-54 (Mar.); Textbook of surgery (Moseley), A-58 (May); Viral and rickettsial infections of man (Rivers), A-64 (Jan.)
Brain, abnormality and mental deficiency, 363; neurosurgical disorders in infants and children, 57; tumor, metastatic, in migrainous patient, 417; tumors, diagnostic problems, 405
Breast, cancer, as source of metastatic brain tumor, 417; tumors, diagnosis and treatment, 513
Bronchiectasis, incidence, 95; surgical treatment, 114, 435
Bronchogenic, *see* Lung
Burns, treatment by exposure method, 535

CANCER, as problem in cell behavior, 534; nutritional research and, 308; of breast as source of metastatic brain tumor, 417; of breast, diagnosis and treatment, 513; of kidney, methods of diagnosis, 9; of lung, incidence, 99; of lung, surgery, 115; of skin and radiodermatitis, 133; of stomach, present status of treatment, 529; of thyroid, 137; of thyroid and pregnancy, A-20 (June); of thyroid, effect of radioactive iodine on, 527
Central nervous system, *see also* Brain; Poliomyelitis; neurosurgical disorders in infants and children, 57
Children, *see* Pediatrics
Chlorine, disinfection of water and sewage, 297
Constipation and irritable bowel syndrome, 32
Contraception, relation to disturbances of sexual function, A-22 (June)
Coronary thrombosis, *see* Heart disease, coronary
Cortisone, effect in allergy, 383; indications in childhood, 557
Cramps of leg in pregnancy, 404
Cushing's syndrome, *see* Adrenals

DEAFNESS, types of hearing impairment, 563
Dermatitis, *see* Skin disease
Diabetes mellitus, coma in, treatment, 164; pregnancy and, A-30 (Jan.)
Diet, following massive resection of small intestine, 79; for patients with dermatitis due to food allergy, 28; low sodium in heart disease, 347; meat, mineral-enriched, as milk substitute, 461
Digitalis, indications in pregnancy, A-20 (June)
Disease, antiquity of, 579
Diuretics, *see* Aminophylline
Drugs, disguising taste of, 562; effect on blood and bone marrow, 185
Dyspnea, "cardiac asthma," 89

EAR disease and role in hearing impairment, 563
Eclampsia, treatment, 402
Elastosis senilis possibly due to Werner's syndrome, A-30 (Jan.)
Electrolysis for removal of hair, A-28 (May)
Embolism, pulmonary, incidence, 98
Environment, and physiology, 299; control in industry, 325
Epilepsy, in children, surgical treatment, 62; treatment with new drugs, 560
Eye, *see also* Vision; disease, detachment of the retina, 107; disease, glaucoma, 2; irrigation, 110; retinal signs of hypertension, 239

FALLOPIAN tubes, inflammation as cause of acute abdominal pain, 24
Fat emulsions in intravenous feeding, 306
Fluorine, effect on dental caries, 294
Fluoroscopy, *see* Roentgen rays
Foreign bodies, removal, surgical, with aid of stereoscopic fluoroscopy, 123
Fractures involving distal epiphysial cartilage of radius, 39
Fluid, parenteral therapy in pediatrics, 70
Fracture of ribs, 112
Fungous infection of lung, incidence, 96

GALACTOSEMIA, treatment with milk-free diet including mineral-enriched meat, 461
Gallbladder, disease as cause of acute abdominal pain, 19; inflammation, chronic, 81
Gamma globulin, passive immunization with, 560
Geriatrics, heart disease, valvular, in aged, 101
Gesell, Arnold, Men of Medicine, 179
Gingiva, bleeding, as diagnostic sign, 100
Glaucoma, prevention of blindness due to, 2
Goiter, *see* Thyroid disease
Granuloma, eosinophilic, 228
Guthrie Clinic Issue, preface, 1
Gynecology, health problems of mothers and children, 309

HAIR, superfluous, removal by electrolysis, A-28 (May)
Hand, dermatitis due to food allergy, 26
Harvard School of Public Health (photographs), 313
Headache, *see also* Brain; migraine, complicating diagnosis of brain tumor, 417
Heart, catheterization, 151; disease and nutrition, 307; disease, congenital, in infants, 141; disease, coronary, anxiety symptoms after, A-28 (Apr.); disease, coronary, emotional factors in, 487; disease, coronary, evolution of myocardial infarction, 459; disease, dyspnea in, "cardiac asthma," 89; disease in pregnancy and labor, 454; disease, rheumatic, care in later life, 358; disease, rheumatic, prophylaxis, 155; disease, salt depletion syndrome during therapy, 547; disease, therapy of failing heart, 344; disease, valvular, in older people, 101
Hemorrhage, *see* Peptic ulcer; Pregnancy
Hepatic, *see* Liver
Hepatitis, *see* Liver inflammation
Hernia, diaphragmatic, 115
Hip, osteoarthritis, surgical treatment, 495
Histamine, *see* Antihistamines
Histoplasmosis, transmission, 296
Hobbies, waiting room, A-40 (Mar.)
Hyaluronidase as aid to hypodermic injection, 560
Hypertension, *see* Blood pressure, high

ILLUSTRATION, photographic exhibit, 443
Industrial medicine, health problems in industry, 323
Infants, *see* Pediatrics
Intestines, irritable bowel syndrome, 32; obstruction, 194; obstruction as cause of acute abdominal pain, 24; sigmoidoscopy, 49; small, medical management following resection, 77; volvulus of midgut in adult due to nonrotation, 45
Instruments, surgical, sterilization of knife blades, A-24 (Feb.)
Iodine, radioactive in management of goiter, 523; radioactive, in treatment of thyroid disease, 137

KELOIDS, removal, A-24 (Feb.)
Kidney, disease as cause of acute abdominal pain, 23; function tests, 122; polycystic, A-36 (Mar.); tumors, methods of diagnosis, 9

LABOR, conduct of, in cardiac patient, 457; conduct of, podalic version and extraction, 201; conduct of, postpartum hemorrhage, 121
Letters from abroad, A-18 (Jan.); A-18 (Feb.); A-22 (Mar.); A-18 (Apr.); A-12 (May); A-12 (June)
Libido, loss of, A-28 (Jan.)
Liver, cirrhosis, 449; enlargement in infants and children, 469; inflammation and infectious mononucleosis, A-34 (Mar.); inflammation, viral hepatitis, A-28 (May)
Lung, cancer, bronchogenic carcinoma, early recognition, 214; cancer, incidence, 99; damage from environmental factors, 299; disease, *see also* Pneumonia; Tuberculosis; disease, changing epidemiologic patterns, 92; embolism, incidence, 93; emphysema, chronic, pneumoperitoneum for, A-30 (Jan.); emphysema, 98; surgery, 111; surgery for bronchiectasis, 435

MALARIA control in tropics, 341
McCormick, Edward J., Portraits and personalities, A-36 (May)
Meat, mineral-enriched, as milk substitute, 461
Medical education for careers in public health, 281
Medical history, antiquity of disease, 579
Medicine, *see also* Industrial medicine; Military medicine; Tropical medicine; practice of, changing medical scene, 274; practice of, environmental factors and, 299; preventive, physician's role in, 287
Men of Medicine, Gesell, Arnold, 179; Wechsler, Israel Spanier, 380
Mental deficiency in children, 363
Microbiology, research in, 331
Military medicine, environmental problems in, 302
Milk substitute, mineral-enriched meat, 461
Methemoglobinemia in infants given polluted water, 293
Mononucleosis, infectious and hepatitis, A-34 (Mar.)
Motion sickness, remedies for, A-28 (May)
Myocardial infarction, *see* Heart disease, coronary

NARCOTICS and sexual impotence, A-24 (Feb.)
Nerves, *see* Central nervous system; Neuritis; Sympathectomy; Vagotomy
Neuritis, serum, following antitetanus injections, 210
Nitrates, poisoning, methemoglobinemia in infants, 293
Neuroses, diagnostic technics, 221
Nutrition, after massive resection of small intestine, 77; deficiency, effect of calorie lack, 238; research in public health, 304

OBESITY, nutritional research and, 307
Oxygen, therapy of heart disease, 345

PANCREAS, inflammation, acute and chronic, 261
Parenteral fluid therapy in pediatric patients, 70
Pediatrics, *see also* Poliomyelitis; eczema, infantile, 253; health problems of mothers and children, 309; heart disease, congenital, in infants, 141; mental deficiency in children, 363; methemoglobinemia in infants given polluted water, 293; neurosurgical disorders in infants and children, 57; newer drugs and their indications, 552; parenteral fluid therapy, 70; peptic ulcer in childhood, 249; streptomycin, indications in infants, A-20 (June)
Penicillin, *see also* Antibiotics; in conjunction with sulfonamides, A-22 (June); treatment of streptococcal infections in children, 153
Peptic ulcer, hemorrhage, medical treatment for, 159; in childhood, 249; perforation as cause of acute abdominal pain, 24; surgery in, 391; vagotomy for, 491
Pericardium, foreign body in, 123
Perspiration, excessive, A-24 (Feb.)
Pheochromocytoma, *see* Adrenals
Photography, medical illustration (exhibit), 443; three dimensional movies for the amateur, A-36 (June)
Placenta previa, 120
Pneumonia, bacterial, incidence, 94; treatment with new sulfonamide mixture, 233
Pneumoperitoneum for chronic emphysema, A-30 (Jan.)
Podalic version and extraction, 201
Poisoning, heavy metal, treatment with BAL, 561
Poliomyelitis, home care, 156; surgery in young patients, 428; virus in water and sewage, 296
Portraits and personalities, Edward J. McCormick, A-38 (May)
Pregnancy, complications, diabetes mellitus, A-30 (Jan.); complications, dyspnea, A-20 (June); complications, heart disease, 454; complications, hemorrhage, 117; complications, leg cramps, 404; complications, thyroid cancer, A-20 (June); complications, toxemia, 402; complications, vaginismus, A-34 (Mar.); ectopic, 120; ectopic, as cause of acute abdominal pain, 24; tests, preservation of hormones during, A-28 (Apr.)
Psychology, medical, mental deficiency in children, 363
Psychosomatic medicine, anxiety symptoms after coronary thrombosis, A-28 (Apr.); diagnosis of neuroses, 221; emotional factors in coronary artery disease, 487
Public health, community health problems, 318; education for careers in, 281; health problems of mothers and children, 309; nutritional research in, 304; physician's role in, 287; physiology and environment, 299; sanitary engineering problems, 292; tropical, importance to world peace, 339

RETINA, arteriolar changes in hypertension, 239; detachment, 107
Rheumatic fever, cardiac sequelae in later life, 358; prophylaxis, 155
Ribs, fracture, 112
Rickettsial infection of lung, 94
Roentgen rays, dermatitis due to, 133; diagnosis of renal tumors, 9; fluoroscopy, stereoscopic, in foreign body removal, 123

SALT depletion syndrome during cardiac therapy, 547
Sanitary engineering, current problems, 292
Sarcoidosis, incidence, 97
Scars, keloid removal, A-24 (Feb.)
Schistosomiasis control in tropics, 342
Senility, premature, A-30 (Jan.)
Sewage disinfection, 298
Sex, function disturbance due to use of contraceptives, A-22 (June); function, impotence and narcotics, A-24 (Feb.); function, loss of libido, A-28 (Jan.)
Sigmoidoscopy, summary of 3500 examinations, 49
Skin, disease, acne, vitamin treatment, A-34 (Mar.); disease, allergic, treatment with cortisone, 389; disease, atopic dermatitis in infant, 252; disease, dermatitis of hands due to food allergy, 26; disease, neurodermatitis, A-36 (Mar.); disease, radiodermatitis, 133; disease, radiodermatitis risk from stereoscopic fluoroscopy, 123; pores, enlargement, A-24 (Feb.); testing and errors in allergy diagnosis, 410
Skull lesions and neurosurgical disorders in infants and children, 62
Sodium, restriction as cause of salt depletion during cardiac therapy, 547; restriction in heart disease, 347
Spermatic cord torsion, 193
Spine, neurosurgical disorders in infants and children, 59, 68
Spleen, excision for blood dyscrasias, 507
Statistics, value, 334
Sterility, treatment, A-26 (Apr.)
Sterilization of knife blades, A-24 (Feb.)
Stomach, cancer, present status of treatment, 529; surgery, *see* Peptic ulcer; ulcer, *see* Peptic ulcer
Streptococcic infections in childhood, 153
Streptomycin, indications in infants, A-20 (June)
Suicide following treatment with antabuse, A-26 (Apr.)
Sulfonamide compounds, indications in childhood, 557; treatment with new triple mixture, 231
Surgery, *see also* Anesthesia; Foreign bodies; Heart; Thorax, and names of specific diseases; instruments, sterilization of knife blades, A-24 (Feb.); orthopedic, in poliomyelitis, 428; postoperative care, effects of early ambulation, 206

TEETH, caries, effect of fluoridated water on, 294
Testes, pain due to torsion of spermatic cord, 193
Tetanus, immunization, A-22 (Feb.); immunization. neuritis following use of serum, 210
Theophylline, *see* Aminophylline
Thorax, *see also* Bronchiectasis; Heart; Lung; Pericardium; surgery, problems, 111
Thyroid, cancer and pregnancy, A-20 (June); disease, 137; hyperthyroidism, radioactive iodine in management of, 523
Tropical medicine, importance to world peace, 339
Trypanosomiasis, control of sleeping sickness in tropics, 342
Trypsin (tryptar) in treatment of infected wounds, 438
Tuberculosis, in children, treatment with new drugs, 556; of lung, incidence, 99; of lung, treatment, 519
Tumors, *see* Cancer; Granuloma
Typhus fever, epidemiology, 333

URINE analysis, reduction of Fehling's solution by normal urine, A-28 (Jan.)

VAGINA, spasm in pregnancy, A-34 (Mar.)
Vagotomy in treatment of peptic ulcer, 491
Varicose veins, examination of patient, 354
Viral infection of lung, incidence, 93
Vision abnormalities, spots before the eyes, A-26 (Apr.)
Vitamins, A and acne, A-34 (Mar.); indications in childhood, 559

WATER, disinfection, 296; supplies, engineering problems, 292
Wechsler, Israel Spanier, Men of medicine, 380
Werner's syndrome as cause of premature senility, A-30 (Jan.)
Wounds, debridement with enzymes, 559; infected, treatment with tryptar, 438

Index to Volume 13
Authors

Anderson, Milton W., Valvular heart disease in older people, 101
Artz, Curtis P., Reiss, Eric, Davis, John H. and Amspacher, William H., The treatment of burns by the exposure method, 535
Augustine, Donald L., Weller, Thomas H. and Thomas, Ruth A., The importance of tropical public health to world peace, 339

Banzet, Paul, Vagotomy in the treatment of peptic ulcer, 491
Baurys, William M., Methods of diagnosis in renal tumors, 9
Blumenfeld, Serge, *see* Lehr, David
Bond, Douglas S., Emotional factors involved in the evaluation of coronary artery disease, 487

Cawley, Edward P. and Wheeler, Clayton E., Granulomas with tissue eosinophilia (eosinophilic granuloma), 228
Chambers, William R., Misconceptions leading to delay in the diagnosis of intracranial space-taking lesions, 405
Clough, Donald M., The acute abdomen: Age and frequency of incidence as aids in establishing the diagnosis, 19
Cole, Harold N., Acute and chronic radiodermatitis as seen in the physicist, physician and dentist, 133
Compere, Edward L., Surgical treatment of osteoarthritis of the hip, 495
Criep, Leo H., I. Effect of adrenals in allergy; II. Effect of cortisone in clinical allergy, 383
Cronheim, Georg, Justice, T. T., Jr. and King, T. Stanton, Jr., A new approach to increasing tolerance to oral aminophylline, 432
Crump, E. Perry, The newer drugs and their indications in childhood, 552

Davey, Winthrop N., Treatment of pulmonary tuberculosis, 519
Davis, John H., *see* Artz, Curtis P.
Denny, Floyd W., Jr., Streptococcal diseases of childhood, 153
Dinsmore, Robert S., Thyroid diseases, 137
Dooley, Samuel W., *see* Kirkwood, Samuel B.
Dotter, Willard E., Fractures involving the distal epiphysial cartilage of the radius, 39
Drinker, Philip, Silverman, Leslie, Yaglou, C. P., O'Connor, Robert B. and MacFarland, Ross A., Industrial health, 323
Dunnington, John H., Detachment of the retina: the Schneider Eye Foundation presentation, 107

Engel, William J., Papilloma of the bladder, 423

Feinberg, Alan R., The antihistamines in treatment of allergic diseases, 266
Fisher, Peter, *see* Shallenberger, Paul L.
Fisher, William A. and Motsay, Dominic S., Parenteral fluid therapy in pediatric patients, 70
Flood, James M., Eczematous dermatitis of the hands due to food allergy: A practical outpatient approach, 26
Friedell, Morris T., Radioactive iodine in the medical and surgical management of goiter, 523

Gale, Joseph W., Problems in thoracic surgery, 111
Garber, Stanley T., Toxemia of pregnancy: Outline of treatment, 402
Gardner, W. James, Neurosurgical clinic, 417
Garvey, John L., Serum neuritis: 20 cases following use of antitetanic serum, 210
Gibson, Glen G. and Peckham, Robert H., Retinal arteriolar signs of hypertension, 239
Gilbert, N. C., The care of old rheumatic cardiac conditions in later life, 358
Girdany, Bertram R., Peptic ulcer in childhood, 249
Goldfarb, Martin L., *see* Lehr, David
Gordon, John E., Leavell, Hugh R. and Ingalls, Theodore H., Solving a community health problem, 318

Heck, Frank J., The influence of drugs on blood and bone marrow, 185
Holden, William D., Splenectomy for blood dyscrasias, 507
Horwitz, Alec, The role of surgery in peptic ulcer, 391
House, Howard P., The hard of hearing patient, 563

Ingalls, Theodore H., *see* Gordon, John E.
Isaac, Peter C. G., *see* Moore, Edward W.
Israel, Harold L., The changing pattern of pulmonary disease, 92

Janes, Robert M., A breast clinic, 513
Johnson, Wingate M., Myocardial infarction—an evolutionary process, 459
Justice, T. T., Jr., *see* Cronheim, Georg

Kanner, Leo, The problem of mental deficiency in children, 363
Katz, Irving A., *see* Palumbo, Louis T.
Kerr, Paul B., *see* Shallenberger, Paul L.
King, Arthur B., Neurosurgical disorders occurring in infants and children, 57
King, T. Stanton, Jr., *see* Cronheim, Georg
Kirkwood, Samuel B., Dooley, Samuel W. and Stuart, Harold C., Health problems of mothers and children, 309
Kleitsch, William P., Trilobectomy and lingulectomy for bronchiectasis, 435
Kusz, C. V., *see* McPheeters, H. O.

Lam, Conrad R., *see* Ziegler, Robert F.
Lawrence, Charles H., Medical management following massive resection of the small intestine, 77

Leavell, Hugh R., The physician's role in preventive medicine and public health, 287
Leavell, Hugh R., *see* Gordon, John E.
Legerton, Clarence W., Jr., Hepatic cirrhosis and its complications, 449
Lehr, David, Terranova, Rosario, Blumenfeld, Serge and Goldfarb, Martin L., Therapy with a new sulfonamide triple mixture: sulfadiazine-sulfamerazine-elkosin, 231
Logan, George B., Significance of hepatomegaly in infants and children, 469
Logan, Victor W., Acute and chronic pancreatitis, 261
Long, Perrin H., *see* Miller, Joseph M.

MacFarland, Ross A., *see* Drinker, Philip
MacKenzie, Walter C., Intestinal obstruction, 194
McPheeters, H. O. and Kusz, C. V., Examination of the patient with varicose veins, 354
Marshall, Samuel F., The present status of the treatment of gastric malignancy, 529
Mazur, Theodore T., *see* Palumbo, Louis T.
Meakins, Jonathan C., "Cardiac asthma," 89
Mercer, Robert D., Recent developments in sickle cell anemia, 224
Miller, Joseph M., White, Beverly H. and Long, Perrin H., Clinical experience with tryptar in the treatment of infected wounds, 438
Moore, Edward W. and Isaac, Peter C. G., Some current problems in sanitary engineering, 293
Motsay, Dominic S., *see* Fisher, William A.
Muench, Hugo, Biostatistics—and why!, 334
Mustard, William T., Surgery in poliomyelitis in infancy and childhood, 428

Napolitani, F. Donald, Three dimensional movies for the amateur, A-36 (June)
Napolitani, F. Donald, Waiting room hobbies, A-40 (Mar.)
Niles, John S., Volvulus of the midgut in the adult due to nonrotation of the intestine, 45

Ochsner, Alton, Early recognition of bronchogenic carcinoma, 214
O'Connor, Robert B., *see* Drinker, Philip

Palumbo, Louis T., Paul, Richard E., Katz, Irving A. and Mazur, Theodore T., Effects of early postoperative ambulation, 206
Paul, Richard E., *see* Palumbo, Louis T.
Peckham, Robert H., *see* Gibson, Glen G.
Peters, John R., Technics in diagnosis of the neuroses, 221
Priestley, James T. and Salassa, Robert M., Lesions of the adrenal glands of surgical significance, 500
Prindle, Ronald E., The prevention of blindness due to glaucoma, 2

Reis, Ralph A., Pregnancy and labor in the cardiac patient, 454
Reiss, Eric, *see* Artz, Curtis P.
Root, Howard F., *see* Stephens, John W.

Salassa, Robert M., *see* Priestley, James T.
Santos, Carlos, Surgical removal of foreign bodies with the aid of stereoscopic fluoroscopy; report of a case involving needle in pericardial cavity, 123
Schmitt, G. F., Therapy of the failing heart, 344
Schnabel, Truman G., Aplastic anemia, 568
Scott, William A., Bleeding during pregnancy, 117
Segal, Harry, Chronic cholecystitis, 81
Shallenberger, Paul L. and Fisher, Peter, Sigmoidoscopy: Statistical summary of 3500 consecutive sigmoidoscopies, 49
Shallenberger, Paul L. and Kerr, Paul B., The irritable bowel syndrome, 32
Shipley, Richard E., *see* Ziegler, Robert F.
Silverman, Jacob J., A simple method for detecting the salt depletion syndrome during cardiac therapy, 547
Silverman, Leslie, *see* Drinker, Philip
Simmons, James S., Education for careers in public health, 281
Snyder, John C., Research in microbiology at the Harvard School of Public Health, 331
Stare, Fredrick J., Nutritional research in public health, 304
Stenn, Frederick, The antiquity of disease, 579
Stephens, John W. and Root, Howard F., Treatment of diabetic coma, 164
Stimson, Philip M., Home care for acute poliomyelitis, 156
Stuart, Harold C., *see* Kirkwood, Samuel B.
Sturgis, Cyrus C., The changing medical scene, 276

Tachau, Paul, Atopic dermatitis in the infant (infantile eczema), 252
Terranova, Rosario, *see* Lehr, David
Thomas, Ruth A., *see* Augustine, Donald L.

Weiss, Gerald N., John Arderne, the father of English surgery, 479
Weller, Thomas H., see Augustine, Donald L.
Wheeler, Clayton E., see Cawley, Edward P.
White, Asher A., Fallacy in allergy, 410
White, Beverly H., *see* Miller, Joseph M.
Whittenberger, James L., Physiology and environment, 299
Wilson, J. Allen, Medical treatment of massive hemorrhage from peptic ulcer, 159
Wilson, Karl M., Comments on podalic version and extraction, 201

Yaglou, C. P., *see* Drinker, Philip

Zeigler, Mildred R., Use of mineral-enriched meats as a substitute for milk in various clinical conditions, 461
Ziegler, Robert F., Lam, Conrad R. and Shipley, Richard E., The diagnosis and treatment of congenital cardiovascular defects in children, 141

* New DRUGS AND INSTRUMENTS

Information published in this department is supplied by the manufacturers of the products described.

• CLYSEROL

DESCRIPTION: New "five minute" enema solution in a disposable 4 oz. plastic container which is also an applicator. The formula is nonabsorptive and contains 1.25 gm. disodium phosphate and 5.83 gm. monosodium phosphate per hundred cubic centimeters of fluid. The knee-chest position is recommended, with retention for approximately five minutes.
PRODUCER: Clyserol Laboratories, 1533 West Reno, Oklahoma City, Okla.

• REDI-POWER TALK-A-PHONE

DESCRIPTION: New 20 watt intercommunication system features Multi-Magic Selector; Dynasonic Universal feature; Hold-a-matic conference control; Unitrans dictation control, and a safety fuse. Capacity of 12, 20, 30 or 40 stations can be housed in the same cabinet with only 12 push-buttons, and the system can be expanded at any time to handle new requirements. Stations may be thousands of feet apart.
PRODUCER: Talk-A-Phone Company, Chicago, Ill.

• MODEL 90A ELECTRIC OXYGEN TENT

DESCRIPTION: Temperature and humidity are automatically controlled as a result of the noncycling refrigeration unit which features an adjustable thermostatic valve that automatically controls the flow of refrigerant into the cooling system. Additional features of the new tent include an adjustable telescopic hangar; an easily viewed dial thermometer; a single control for oxygen flush and flow; an efficient air cleaner and humidifier; a blower motor that is oiled for life; noiseless casters; a sight-glass drain tube, and removable panels.
PRODUCER: Ohio Chemical & Surgical Equipment Co., Madison, Wis.

• PICKER-POLAROID ONE MINUTE X-RAY

DESCRIPTION: Now available for civilian use. Operation is as follows: (1) Load the cassette, in broad daylight if necessary; (2) make exposure with any x-ray source and then slip the cassette into the processing box; (3) wait a minute, then take out a finished, completely dry radiograph.

Complete description and literature available on request to:
PRODUCER: Picker X-Ray Corporation, White Plains, N.Y.

• RAY-X SPONGES

DESCRIPTION: New type surgical sponge with a barium sulfate insert that is x-ray detectable. Inserts are permanently fused to the gauze and do not deteriorate. Sponges can be sterilized in the usual manner.
PRODUCER: Parke, Davis & Company, Detroit, Mich.

• SURDON TABLETS

PURPOSE: Control of premenstrual tension and dysmenorrhea.
COMPOSITION: Each tablet contains 5 mg. PROGESTORAL® (ethisterone), 15 mg. thiamine hydrochloride and 15 mg. phenobarbital.
DOSAGE AND ADMINISTRATION: Recommended average dose is 1 or 2 tablets per day during the last 7 to 10 days of the menstrual cycle.
PRODUCER: Organon, Inc., Orange, N.J.

(Continued on page A-50)

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Each number will contain a Symposium (sometimes two Symposia) on a topic of current interest. The first year's program is as follows: *February*—Cardiovascular Disease; *May*—1) Clinical Advances, 2) Poliomyelitis, 1954; *August*—Care of the Newborn; and *November*—1) Pediatric Accidents and Emergencies, 2) Pediatric Allergy. *Enter your subscription now!*

A special advance number of The Pediatric Clinics will be available early in June, 1953. This advance number takes the form of a *Symposium on Poliomyelitis,* prepared with the editorial assistance of the National Foundation for Infantile Paralysis. It reports on the clinical aspects of recent advances in this field (including gamma globulin and the new vaccine) and contains a precise outline of the diagnosis and management of polio today. This Symposium will be mailed with the compliments of the Saunders Company to all general practitioners and pediatricians. Other physicians may obtain a copy by sending a written request to W. B. Saunders Company.

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Letters from Abroad

FROM POSTGRADUATE MEDICINE'S CORRESPONDENTS

AMSTERDAM

Toxic reactions to isonicotinic acid hydrazide—Severe toxic reactions to isonicotinic acid hydrazide have thus far not been frequently described. The publication of an article by R. L. Baart de la Faille and M. C. Verloop (*Nederlandsch tijdschrift voor geneeskunde* 97:548, 1953) is therefore important. A man with long-standing pulmonary tuberculosis was given 150 mg. of isonicotinic acid hydrazide (NIDATON®) a day orally, beginning May 25, 1952. Blood and urine were examined regularly and were found to be normal. From time to time the therapy was discontinued for a few weeks. Except for administration of vitamins, the patient received no other therapy. From June 25, 1952, 200 mg. of nidaton was administered daily. On September 4, following the administration of 284 tablets of 50 mg., the patient noticed a few petechiae on his legs. The nidaton therapy was immediately stopped. The next day the patient began to bleed profusely from the nose and anus and to cough up blood. The petechiae spread.

On September 6, 96,600 thrombocytes were counted (Fonio method). On September 13 no thrombocytes were found in the smears. Except for new petechiae, further bleeding did not occur. Physical examination was negative. A blood transfusion (400 cc.) was given. On September 15 the number of thrombocytes was 15,600, bleeding time 3½ minutes, coagulation time 4¼ minutes and prothrombin time 24 seconds (control 17 seconds). Without further treatment, the number of thrombocytes once more increased and on November 1 the total was 253,000.

Although it has not been proved, the authors think it likely that the isonicotinic acid hydrazide was the cause of the thrombocytopenic purpura.

Only one other case of purpura following administration of isonicotinic acid hydrazide (RIMIFON®) is known to them to be described in the literature (Collins, *British Medical Journal*, August 16, 1952). In that case, however, the number of thrombocytes was normal.

In the same issue of the *Nederlandsch tijdschrift voor geneeskunde* (page 540) J. Th. Planten describes a case of toxic amblyopia probably caused by ethylpyridine, which is an intermediary product in the manufacture of isonicotinic acid hydrazide. The patient was a 31 year old man who worked for three months in one of the departments of a pharmaceutical factory where ethylpyridine was being distilled in great quantities. Shortly thereafter he complained of his eyesight. Examination disclosed the vision of both eyes to be 5/30, which could not be corrected. In addition there was a central scotoma on either side. On extensive examination no other cause for the amblyopia was found, and a diagnosis of toxic amblyopia as a result of ethylpyridine was made. The therapy consisted of discontinuing work, retrobulbar injections of vasodilative agents, oral administration of vitamin B complex and intramuscular injections of vitamin B_1. A week later the vision had decreased to 5/50. Two months after the first examination, however, the vision had risen to 5/6 and the central scotomas had disappeared. Vitamin therapy was continued. In the factory, the ventilation was improved.

No Dutch neurologists to the fifth International Neurological Congress in Lisbon—The Dutch preparatory committee of this congress, which is to be held in Lisbon in September, has decided to withdraw. This decision, which was preceded by an unsuccessful protest to the Portuguese executive committee, was sanctioned by the Dutch Association of Psy-

(Continued on page A-14)

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chiatry and Neurology. The principal argument is that the German professor, Dr. Hallervorden, is attending as opener in the main discussions. Moreover, the Dutch committee cannot agree to the fact that there are going to be no less than 5 Germans out of 18 openers who will be speaking in the plenary session. In view of the scientific achievements of the Germans, this number is considered out of proportion.

LONDON

British Medical Association—The annual meeting of the British Medical Association will be held this year at Cardiff, the capital of Wales, from July 9 to 17. The president-elect is Dr. J. W. Tudor Thomas, the Cardiff ophthalmic surgeon and pioneer of corneal grafting. A feature of the meeting will be the plenary sessions, three in number: (1) "Coronary Disease," with Professor Scarborough of Cardiff in the chair and with discussions by heart specialists from Cardiff, London, Birmingham and Edinburgh; (2) "Fibrositis," with Dr. Lawrence Abel of London in the chair and with speakers including rheumatism experts and orthopedic surgeons from Cardiff, London and Bath, in addition to a well known general practitioner, and (3) "Overweight," with Lord Horder in the chair and with speakers from Cardiff, Cambridge, Oxford and Edinburgh.

There is again to be a Scientific Exhibition on the lines of those at the A.M.A. meetings in the United States though on a lesser scale. The first such exhibition held in Britain, that presented last year at Dublin, proved a great success. Seventeen scientific sections have been arranged, all with full programs and with varied subjects. Visitors from Canada and the United States will be particularly welcome at Cardiff.

Health Service drugs—The recent report (1951-1952) of the Government Auditor-General shows a shocking waste of money on the prescription of drugs. For example, a proprietary drug used for reducing cost 400,000 pounds (about $1,200,000), whereas exactly the same substance under its standard name would have cost only 158,000 pounds (less than $500,000). Accounts show an excess of more than 7,000,000 pounds over the grant allotted for pharmaceutical services, a great part of which is due to the prescription of new and expensive drugs. The percentage of proprietary medicines prescribed has been increasing steadily. In 1951 this amounted to 23 per cent of the total cost of prescriptions in England and Wales and to as much as 30 per cent in Scotland. A sample analysis in April 1952 showed a further rise of 25.6 per cent in England and Wales.

A recent article by Professor D. M. Dunlop and two colleagues (*British Medical Journal*, March 28, 1953) surveyed the prescriptions issued throughout Scotland during the month of October 1951. The total number was 18,848. The survey points out that more than seven tons of cotton wool are ordered annually in Scotland under the National Health Service, and the total cost of prescriptions in Scotland during this one month was 412,500 pounds. Vitamins, tonics and such symptomatic remedies as sedatives, hypnotics, analgesics, cough mixtures, stomachics and laxatives constituted 51.6 per cent of all prescriptions, and the large proportion of these drugs must be considered mere placebos. Many of them cost more to compound and pack than the value of the drugs themselves. Vitamins were prescribed more often than iron, and constituted about 5 per cent of all prescriptions. During the month liver extract was ordered 125 times, compared with only 97 prescriptions for insulin and 134 for digitalis, but the authors comment that the recent 1 shilling charge on prescriptions may be justifiable as a mild mass deterrent, though it is unfortunate that it penalizes the chronically ill persons without greatly discouraging the hypochondriac with a passion for medicine.

Deaths from fog—During the severe fog in Greater London in the week ending December 13, 1952, nearly 3000 persons died from diseases directly attributable to the fog. One of the most remarkable series of deaths was that of prize cattle at a fat stock show. The animals caught bronchitis and were so fat that they were unable to lie down, resulting in a high rate of mortality. The fog was of the "smog" type rather than the old-fashioned London "pea soup" variety, and the reason for this has not yet been ascertained. It is understood that the Atmosphere Pollution Research Committee set up by the government is making an urgent study of the problem.

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Your Questions answered

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• PREGNANCY AND THYROID CANCER

Question: A 40 year old housewife, gravida 6, para 5, has undergone unilateral lobectomy with removal of involved satellite lobes of the thyroid for carcinoma of that gland. She is still fertile, having been confined twice in the past two years. Is there evidence that future pregnancy would be detrimental to such a patient? The patient and her husband request sterilization. Is there a medical basis for tubal ligation?

M.D.—Iowa

ANSWER: There is no question but that enlargements of the thyroid do commonly occur during or shortly after pregnancy. Most of these are cases of lymphoid thyroiditis, but I have seen several instances in which carcinomas have appeared in association with pregnancy and have seemed to enlarge quite rapidly during or shortly after pregnancy. I do not know that a definite relationship can be established, nor would I think that the presence of a carcinoma of the thyroid itself would be an indication for sterilization. Certainly it would be a good indication for contraceptive instruction.

GEORGE CRILE, JR.

• STREPTOMYCIN FOR INFANTS

Question: What are the indications for the use of streptomycin in an infant 2 months of age, excluding tuberculous disease?

M.D.—Illinois

ANSWER: The indications for the administration of streptomycin to a 2 month old infant would be the same as for an adult. Streptomycin would be used for influenzal meningitis, for influenzal infections of the upper part of the respiratory tract, for infections of the urinary tract due to gram-negative organisms when the orally administered broad spectrum antibiotics and sulfonamide drugs cannot be used, and perhaps in the rare case of bacterial endocarditis, either alone or together with penicillin or terramycin, as indicated on the basis of the organisms that were isolated.

• USE OF DIGITALIS

Question: A 28 year old woman, mother of five small children, consulted me on November 17, 1952, complaining of a sore back. She was in the fourth month of pregnancy. Her previous deliveries had been uncomplicated, and labor and puerperal periods uneventful. She had begun menstruating at the age of 12 years, and her menstrual periods had been regular, at 28 day intervals. The flow continued for seven days, and was normal in amount. There had been no dysmenorrhea. I had not seen her during her previous pregnancies.

Her temperature was normal. Hemoglobin was 75 per cent. The Kahn test was negative. Pelvic measurements were normal, and urine was negative. Rh factor was positive. Blood pressure 102/70. Three days later she consulted me because of shortness of breath, and stated that this had been present with each previous pregnancy. Her pulse was regular (84) and there was no edema. I gave her tablets of digisidin 0.1 mg. to be taken before breakfast each day, and instructed her to report back in a week. At her first visit I had given her a pregnancy diet list, and prescribed vitamin capsules.

Her next visit was December 29, 1952. Her hemoglobin measured 65 per cent, and she had a severe cough. I gave her 600,000 units of penicillin and prescribed digisidin in the same dosage as before. I told her to report back in a week.

Am I justified in prescribing digitalis and, if

(Continued on page A-22)

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so, in what strength and how often? Some say that you may do a patient more harm than good if you give digitalis for shortness of breath without edema of the ankles and positive urinary findings. Your opinion will be appreciated.

M.D.—Michigan

ANSWER: Digitalis would not be indicated in this case if the patient's dyspnea is due to something other than early congestive failure, or to a lowered myocardial reserve. If her shortness of breath is due to a pulmonary process which resulted in the severe cough described, plus the added factor of anemia, the use of digitalis would not be indicated. From the data at hand, there is no good evidence that she has primary myocardial involvement. Although severe cough is typical of a marked mitral stenosis, the latter condition, if present, would have been mentioned in the protocol, and even this would not explain the rather marked anemia which was found.

In a general way, the use of digitalis is indicated for patients who have enlarged hearts and lowered cardiac reserves, even though frank congestive failure with edema has not developed. It is only in persons with hearts of normal size and apparently normal output that the use of digitalis would tend to decrease somewhat an output which already is adequate. It is unlikely, however, that the effects of digitalis in such a situation would be clinically apparent.

• DISTURBANCES OF SEXUAL FUNCTION

Question: Has any definite relationship been established between the practice of the prevention of conception by the male's using various mechanical equipment such as the condom or by the woman's use of suppositories or other technics and causation of harmful disturbances of function? Many patients have raised this question. While I have never heard of any scientific studies, I would be much interested to know if proof has been developed on this subject.

M.D.—Iowa

ANSWER: The answer to this question of disturbance of function is rather difficult. It is quite hard to determine whether the inquiry has to do with the normal function of the sexual organs, both in the male and female, or whether he refers to the normal function of sexual intercourse.

In the male, condoms are used because the female partner is afraid that conception will occur and she may insist not only that the condom be worn by the male partner, but also that withdrawal be practiced. In this way, there is a disturbance of function, in that the female partner does not get the satisfaction that she should have and that is necessary for the normal functioning of the organs taking part in normal sexual intercourse. A great part of this, of course, is mental fear.

In my own experience, when I find it necessary to prescribe methods of contraception, I insist that the partners have normal sexual intercourse, that the act be completed and satisfying to both the male and female. In this way, I feel that disturbance of function may, and usually does, not occur. Disturbances of normal sexual function may occur more in the female than the male. Many times the use of condoms that interfere with normal sensations may prevent the climax of the partners occurring when it should, simultaneously. I think a physician who prescribes contraceptives should instruct the individuals how to use them. Certain instructions should suggest what normal intercourse is, and, if this is not attained, that the contraceptive appliance may interfere with normal function.

A recent report reveals that chronic congestion of the posterior urethra, in males, may occur when coitus interruptus is practiced continuously. This interferes with normal sexual function in the male.

GILBERT J. THOMAS

• PENICILLIN

Question: 1. Will the injectable type of procaine penicillin be satisfactory when mixed with a sulfonamide suspension?

2. Is this superior to crystalline penicillin?

3. How long will it keep its potency?

M.D.—Michigan

ANSWER: 1. When penicillin and sulfonamides are given in combination, it is best to give them separately rather than in mixtures.

2. When penicillin is given orally, crystalline penicillin G is preferable to procaine penicillin.

3. The expiration dating period of procaine penicillin is 24 months after the particular batch has been certified.

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MEDICAL *Miscellany*

Three Dimensional Movies for the Amateur

F. DONALD NAPOLITANI

New York City

ALTHOUGH three dimensional silent movies were first exhibited at the New York World's Fair in 1939, I first had the pleasure of watching such movies made by amateurs at the 1952 convention of the Photographic Society of America in New York City.

The simplicity of using an amateur 16mm. moving picture machine, such as the BOLEX, interested me in delving further into the subject. especially when it meant merely obtaining attachments which, when used in photographing surgical operations, would give new life and depth to the surgical field. This is true to such an extent that the viewer can feel that he was present at the operation itself.

For those interested in the theory and technic involved in the use of stereo-optics and moving picture making, the following is a brief outline: The image must be represented to the machine as though seen by both the right eye and the left eye. Naturally, a separate lens is used to represent each eye. The individual images are used together to give the depth which we all know exists in bi-optic vision.

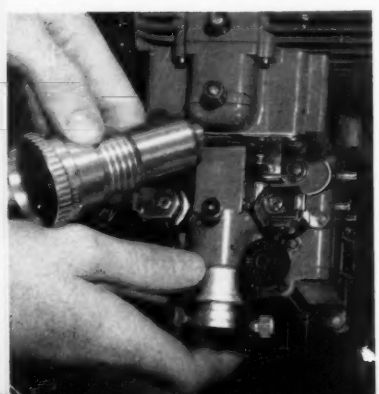
Try this experiment: Close one eye and hold your right forefinger 10 inches in front of you. Now, with the one eye closed, attempt to touch the second finger of your left hand against the finger which is held in front of you. The reason you cannot do so is that you do not have depth perception. The same situation will exist if you close the opposite eye and employ the same technic. However, the moment you open both eyes you are fusing the picture of the two fingers in front of you so that you can ascertain the distance away from your head. Then it is easy to place one finger against the other.

To make three dimensional sound movies, the first step is to equip the Bolex H-16 camera with a stereo lens. Single perforated (sound) film should be used.

Hence, a 2½ lens is used to represent both eyes. This is regulated to photograph the image twice on the 16mm. film. Therefore, the final picture will be an oblong rather than a flat type of picture. Ordinary 16mm. film, either black and white or color, is used. A focal length of 20mm. is then used to project these two images onto a screen. At the time you photograph an operation, then, instead of placing one picture of the operation on each 16mm. frame, you are cutting your frame in half and employing two pictures; this is effected by using the Bolex attachment in front of an ordinary 16mm. machine.

The film is processed in the usual manner, no special technic being required. The lens used is fast enough so that limited color work may be done even at night. The objects photographed may be taken stereoscopically at distances of 5 feet to infinity. Closeup attachments are also available. When the film has been developed, a

(Continued on page A-38)



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* **Oster, K. A., and Golden, M. J.: Exp. Med. & Surg., 7:37, 1949**
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special attachment is placed before the projector. Ninety per cent of all modern machines for sound or silent projection will accommodate this single unit lens attachment which is a special duplex Kern-Paillard fl. 6 lens.

The special lens is used so that the two pictures on the special frame film will fuse together at the twist of the dial attachment. This can be done easily since you have removed your present projection lens on your projector and have inserted the new projection attachment. Nothing will go wrong and there is nothing delicate to adjust. When the pictures are flashed onto the screen, both images are fused together and a POLAROID® viewer will fuse the two pictures to produce a direct image which shows depth.

In the study of surgical operations and other medical conditions, this new camera technic will be of great value in forwarding the progress of medicine. Recently in New York a special type of screen with a curved area has been demonstrated, but it is not practical for amateur work. Work is being done in a foreign country toward the development of a stereoscopic technic without the use of a polarizing lens but with little success as yet.

In stereoscopic photography it is suggested that lighting be arranged in front of the object rather than from the side or the back. Due to the oblong type of picture resulting, the use of a silver screen is recommended. This can be made by painting a surface of canvas; special silver screens can also be obtained commercially.

If the amateur photographer is interested in having sound with his film strip, the Bell & Howell Company will add magnetic "sound stripe" strips to the edge of the film after it is processed. The film is then ready for recording of the sound track on the Film-O-Sound magnetic recording projector. However, I feel that the richness and realism resulting from the stereoscopic film itself will more than compensate for a lack of sound along with the picture. In using this technic to record operations or to show a patient where a tumor is palpated, etc., the realism and depth attained are striking. The present high cost of attaching sound to the film should not deter the amateur's enthusiasm.

Amateur operators may obtain further information from Mr. Thomas Elwell, Paillard Products, Inc., 265 Madison Avenue, New York 16, New York.

The Medical Muse

RICHARD ARMOUR

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More of a stoic sort than she
Who chose to marry an M.D.
She keeps the books, makes out the bills,
And holds her tongue on patients' ills.
She waits the dinner as she's told,
Then eats it by herself, and cold.
And mostly staying home alone
And answering the telephone,
She says the doctor (here's the prize)
Will soon be there—and knows she lies.

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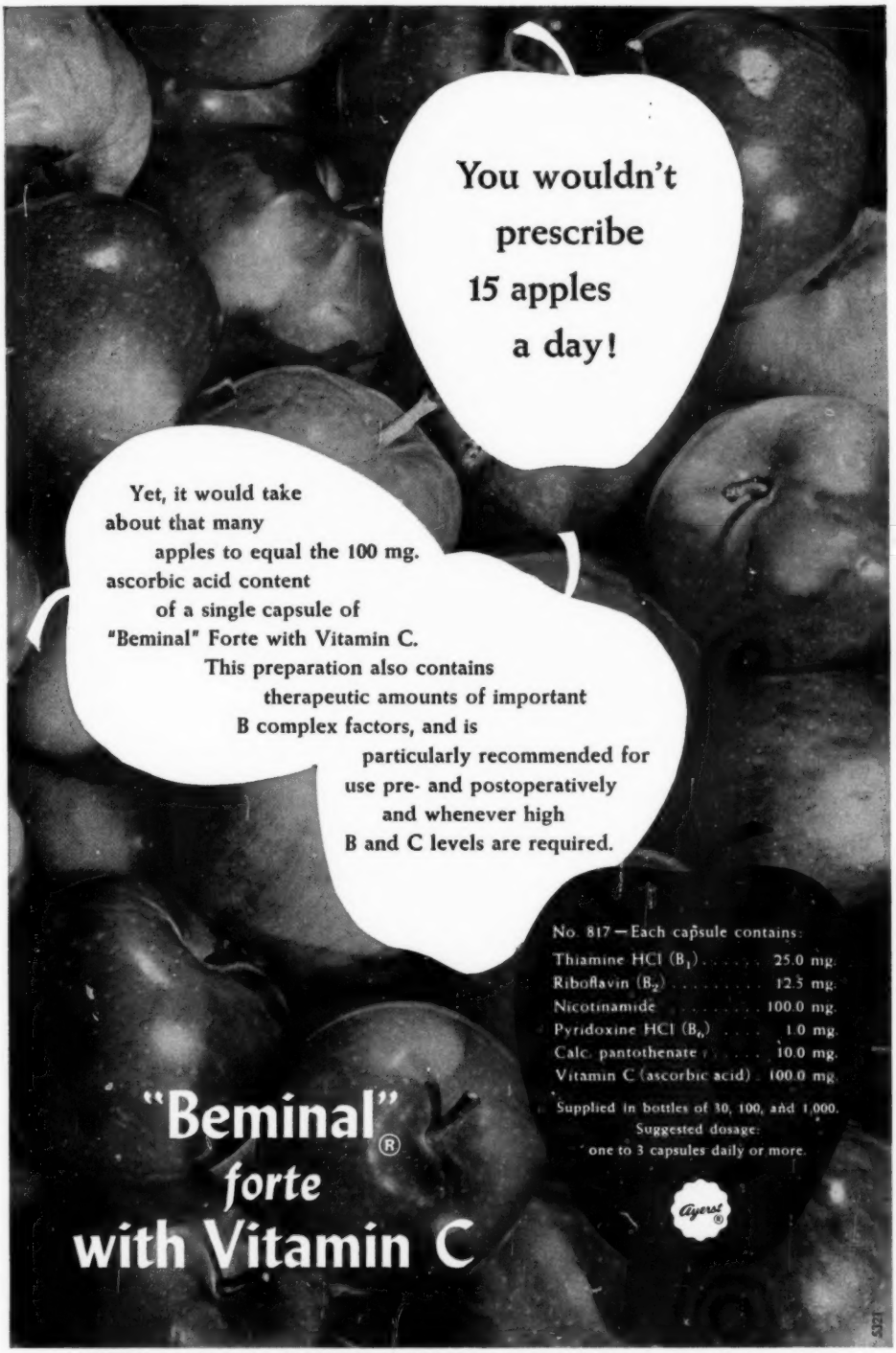
He's never sick on Saturdays,
In fact this wondrous, welcome wight
Is also never sick at night.
In waiting rooms he does not burn
But gladly sits and waits his turn,
And even, I have heard it said,
Begs others, "Please, go on ahead."
He takes advice, he does as told,
He has a heart of solid gold.
He pays his bills, without a fail,
In cash, or by the same day's mail.
He has but one small fault I'd list:
He doesn't (what a shame!) exist.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THE MEDICAL Bookman

► GYNECOLOGICAL AND OBSTETRICAL PATHOLOGY

By Peter A. Herbut, M.D., Professor of Pathology, Jefferson Medical College, Philadelphia. 683 pages with 246 figures and 2 color plates. 1953, Lea & Febiger, Philadelphia. $12.50.

The author states in the preface that this book is written for the undergraduate medical student, general practitioner, gynecologist, obstetrician or pathologist. It goes without saying that all but the pathologist will find a great deal of useful information in this book. In addition to the extensive sections devoted to pathology, there are shorter sections on clinical manifestations as well as on diagnosis and treatment. These excellent, though brief, additions to the text give the book a well rounded gynecologic content and a pleasing readability.

Pathologists will probably find much useful information in the book, but the material is perhaps not complete enough to satisfy all physicians in the field of pathology. The excellent chapters on cytology, Rh factor and blood groups make profitable and instructive reading to all physicians interested in gynecologic conditions.

The book has many fine illustrations and is well printed.

R. E. E.

► BACTERIAL AND MYCOTIC INFECTIONS OF MAN

Edited by Rene J. Dubos, Ph.D., The Rockefeller Institute for Medical Research. Ed. 2. 886 pages with 98 illustrations. 1952, J. B. Lippincott Company, Philadelphia. $7.50.

This is a companion piece to Rivers' "Viral and Rickettsial Infections of Man." Dr. Dubos, with the assistance of 36 associates, has covered the field of medical microbiology and immunology with a minimum of overlapping into the virus field. An appendix lists materials and methods of preparation and includes a simplified guide to recognition of bacteria. Bibliographic and subject indexes are adequate.

Each chapter is considered as an entity and carries its own reference material. A great deal of data have been condensed into tabular form, and well chosen photographs and charts clarify the text throughout. Medical microbiology is the study of host-parasite relationships rather than of the bacteria or of molds as individual entities. It is concerned with the structure and properties of the parasites which play a part in their pathogenic behavior and the manifestations developing following invasion. The information obtained during the four years since the appearance of the first edition warrants publication of this second edition. Discussions throughout are practical, although the theoretical background is included as a basis for considering the nature of infections and the treatment. Treatment and epidemiology are considered in connection with each section of this book.

J. C. M.

► ELECTROCARDIOGRAPHY IN PRACTICE

By Ashton Graybiel, M.D., U.S. Naval School of Aviation Medicine, Pensacola, Florida; Paul D. White, M.D., National Advisory Heart Council; Louise Wheeler, A.M., Cardiac Laboratory, Massachusetts General Hospital, and Conger Williams, M.D., Harvard Medical School. Ed. 3. 378 pages with 294 figures. 1952, W. B. Saunders Company, Philadelphia & London. $10.00.

This well known book has now been thoroughly revised, taking into consideration new developments in clinical electrocardiography, and it

(Continued on page A-56)

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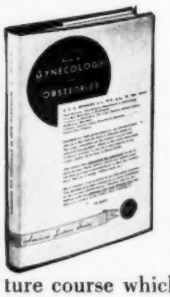
has been amplified by numerous new instructive illustrations. In its introductory part the physiologic principles of the electrocardiogram and the mode of operation of a galvanometer are described in an original way based on historical developments. Methods of recording and the application of various electrocardiographic leads and their relationship to the spatial vectorcardiogram are explained, and the variations of the normal electrocardiogram are dealt with in two subsequent chapters. This is followed by a presentation of the principal manifestations of disorders of the cardiac rhythm and of intraventricular conduction. The three following chapters deal with more or less specific alterations of the electrocardiogram and with typical etiologic patterns. Finally 36 representative electrocardiograms are included together with case histories for exercise in electrocardiographic diagnosis.

As in previous editions the principal aim of the authors is directed toward a complete yet simple presentation. This is achieved by a concise and clearly written text and by excellent reproduction of carefully selected illustrations. Thus the new edition truly fulfills its stated purpose—to be an atlas, not a textbook, of electrocardiography, containing many electrocardiograms primarily devoted to the interests of the practitioner.

L. N. K.

► PHYSIOLOGICAL BASES OF GYNECOLOGY AND OBSTETRICS

By S. R. M. Reynolds, Ph.D., Department of Embryology, Carnegie Institution of Washington. 153 pages. 1952, Charles C Thomas, Springfield, Illinois. $5.50.



Dr. Reynolds has put in book form his lectures on the physiologic bases of obstetrics and gynecology (gynecotokology). The author graciously acknowledges the kindness and assistance given him by various individuals. In the foreword he gives an outline of his lecture course which covers 15 separate topics.

The author states that his concept is that there are three physiologic mechanisms of the uterus and that they are interrelated and interdependent. These three mechanisms are uterine growth, uterine motility and uterine vascularity.

The basis of the onset of labor, the strength of fundal contraction, the action of actomyosin and its dependence on an activator are discussed. The dilation of the cervix and its physiologic basis are described. Menstruation is ascribed to a series of integrated factors resulting from both the special morphologic and physiologic characteristics of the endometrium.

The action of estrogenic hormone and of progesterone on the ovarian vasculature and on the function of the ovary and the endocrine effects of hysterectomy are also described.

There is a logical description of uterine growth and uterine circulation during pregnancy. Fetal maturity at birth and the reasons for the onset of labor are discussed.

The series of lectures is thought-provoking and well worth reading by the clinician.

R. D. M.

► BIOCHEMISTRY OF DISEASE

By M. Bodansky and O. Bodansky. Ed. 2, thoroughly revised and enlarged, by Oscar Bodansky, M.D., Professor of Biochemistry, Sloan-Kettering Division, Cornell University Medical College, New York. 1,208 pages. 1952, The Macmillan Company, New York. $12.00.

Oscar Bodansky has done a very effective job of revising the first edition prepared with his late brother Meyer. During the 13 years since the first edition of their reference book appeared in 1940, there have been rapid and extensive changes in biochemistry and the application of its technics to recognition of disease states and of the improvement or failure of body functions.

The book follows an orderly plan, presenting biochemical considerations associated with diseases of the blood, heart and cardiovascular system, respiratory, renal and genitourinary tracts, the digestive system, and the liver and biliary tract. It then passes to a consideration of the endocrine glands, specifically segregating the pancreas, adrenals, pituitary, thyroid, parathyroid and male gonads. Diseases of the bone and of muscle are then discussed. A courageous chapter discusses the applications of biochemistry in obstetrics and gynecology. Miscellaneous disorders of nutrition and metabolism are considered in some detail, and the book closes with a great deal of new information in connection with bio-

(Continued on page A-58)

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chemical aspects of neurologic and psychiatric disorders.

Finally, normal clinical biochemical values are assembled in an appendix which gives consideration to statistical evaluation of the normal range. Each chapter has its own bibliography, and the last 26 pages carry a subject index with close references to chemical components.

This should be an interesting and helpful book to the biochemist, the general practitioner, the internist, the obstetrician, the gynecologist and the psychiatrist.

J. C. M.

► 1952 YEAR BOOK OF DRUG THERAPY

Edited by Harry Beckman, M.D., Director, Departments of Pharmacology, Marquette University Schools of Medicine and Dentistry, Milwaukee. 606 pages, illustrated. 1952, The Year Book Publishers, Inc., Chicago. $5.50.

The care spent in preparing this annual Year Book indicates either a labor of love or a love of labor!

Summarized are over 500 papers which were published during the preceding year. The table of contents indicates their classification in the fields of allergy, antibiotics, cardiovascular diseases, dermatology, endocrinology, hematology, internal medicine, neuropsychiatry, obstetrics, ophthalmology, pediatrics, surgery and venereology. An author index covers 116 pages, and a very adequate subject index 27 pages more.

The reviews appear adequate as well as comprehensive. The particular value of this publication, however, lies in the footnotes and comments by the editor, who indicates the importance of the publication and ties it to previous reports in the same field. It is difficult to indicate the outstanding features in this excellent summary. The work on ACTH and cortisone therapy in rheumatoid arthritis, the use of broad spectrum antibiotics in fungous infections, the value of AUREOMYCIN® in bacterial pneumonias, the persistence of penicillin in the tissues, the use of alcohol as an antifoaming agent, the growing frequency of agranulocytosis, a continuing polemic regarding the mechanisms of action of digitalis in congestive failure, the necessity for continuing blood studies in the use of new anticoagulants, the development of new diuretics, new drug therapy for helminth infection, new treatments for morphine addiction, products superior to cortisone in rheumatoid arthritis, new antithyroid drugs safer than propyl thiouracil—who can say which of these is the most important?

J. C. M.

► DISEASES OF THE HEART AND ARTERIES

By George R. Herrmann, M.D., Professor of Medicine, University of Texas. Ed. 4. 652 pages with 215 figures and 4 color plates. 1952, C. V. Mosby Company, St. Louis. $12.50.

Although a number of very good books recently have appeared in the field of diseases of the heart and arteries, there has long been a need for a concisely written text such as this, which provides the undergraduate with a basic understanding of the whole field. During the 16 years since the first appearance of the book, many changes have occurred in the science of cardiology and all the important ones are included in the current edition.

The arrangement follows a logical method of presenting the subject to the student and permits the practicing physician to find the material he seeks easily. Chapters on instruments and methods used in clinical heart studies will be especially helpful. A chapter on radiologic study of the heart serves as a good introduction to the subject, although it would have been more helpful to have a more comprehensive review of this method, which is assuming greater importance in a complete examination of the heart. Electrocardiography is clearly and fully explained in the long chapter devoted to the subject.

Succeeding chapters follow the traditional pattern of discussion of cardiac irregularities, classification in which the American Heart Association standards have been used, and review of various etiologic entities of heart disease. The book is written from a clinical standpoint, and basic facts from the past as well as recent reports are skillfully interwoven.

The section on peripheral vascular diseases is short and contains most of the pertinent clinical material for a book of this type. It was especially gratifying to find chapters on nervous disorders with cardiac manifestations, treatment of emergency conditions of the heart and blood vessels, military cardiology and, finally, an excellent

(Continued on page A-60)

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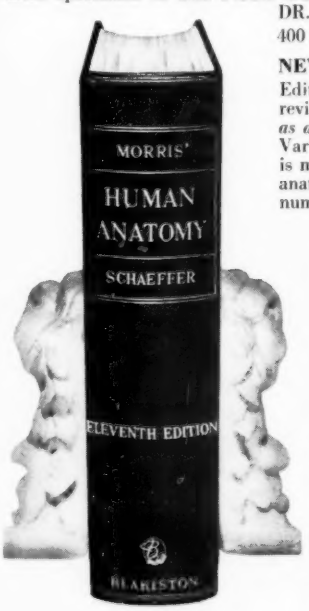

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summary on the diagnosis of heart disease. There are many original drawings and some color plates that help clarify points mentioned.

H. C. L.

► ADVANCES IN INTERNAL MEDICINE

Edited by William Dock, M.D., Long Island College of Medicine, Brooklyn, and I. Snapper, M.D., The Mount Sinai Hospital, New York. Vol. 5. 464 pages, illustrated. 1952, The Year Book Publishers, Inc., Chicago. $10.50.

Nine comprehensive and current reviews of phases of medicine receiving considerable attention in the last few years comprise this volume. Most of the subjects presented are of clinical interest and hence diagnosis and treatment make up a goodly share of each article, although the more basic aspects are fully covered as well.

Included are reviews on cardiac catheterization, portal hypertension, gout, anemia of infection, multiple myeloma, influenza and maternal diseases affecting the offspring. Sections of particular clinical interest deal with ganglionic and adrenergic blocking drugs and the use of adrenocorticotropic hormone and cortisone.

All the articles are thorough in presentation but may stress one or more phases of the particular subject. In the cardiac catheterization section, technic, physiologic principles and abnormal hemodynamic findings in congenital and acquired heart disease are emphasized along with numerous helpful explanatory diagrams which record flow rates, pressures, and oxygen content in the various vascular chambers and circuits. Results of catheterization of renal and hepatic vessels are also presented and discussed.

The surgical treatment of portal hypertension and normal hepatic circulation are stressed while the multiple myeloma article deals exclusively with changes in the proteins in myeloma. The epidemiology and prophylaxis of influenza are fascinating subjects and comprise the bulk of the chapter devoted to influenza.

The reviewer found the lead article by Dr. Murray H. Bass of Mount Sinai Hospital, New York, on maternal illnesses in their relation to infant anomalies and illnesses of exceptional value. Data collected from the journals of many specialties are combined in a most informative and readable manner.

T. B. G.

Books received will be acknowledged in this department each month. As space permits, books of principal interest to our readers will be reviewed more extensively.

Diagnostic Tests in Neurology; A Selection for Office Use. By Robert Wartenberg, M.D. Forewords by Sir Gordon Holmes, M.D. and Stanley Truman, M.D. 228 pages with 62 figures. 1953, The Year Book Publishers, Inc., Chicago. $4.50.

Pathology of the Heart. By S. E. Gould, M.D., Clinical Professor of Pathology, Wayne University College of Medicine, Detroit, Michigan, and collaborators. 1,023 pages with 690 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $25.50.

Ménière's Disease. By Henry L. Williams, M.D., Consultant in Section on Otolaryngology and Rhinology, Mayo Clinic, Rochester, Minnesota. 349 pages with 15 illustrations. 1952, Charles C Thomas, Springfield, Illinois. $7.00.

The Psychopathic Delinquent and Criminal. By George N. Thompson, M.D., Associate Clinical Professor of Neurology and Psychiatry, School of Medicine, University of Southern California. 157 pages with 20 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $4.50.

Overeating, Overweight and Obesity. Proceedings of the Nutrition Symposium, Harvard School of Public Health, Boston, October 29, 1952. By David P. Barr, John R. Brobeck, Henry W. Brosin, Louis I. Dublin, Frank A. Evans, P. C. Fry, Samuel Gurin, Paul György, Edward E. Hunt, Jr., Ancel Keys, P. S. Peckos and A. W. Pennington. Nutrition Symposium Series, No. 6. 151 pages. 1953, The National Vitamin Foundation, Inc., New York. $1.50.

Hypersplenism; A Clinical Evaluation. By Cyrus C. Sturgis, M.D., Director, Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan, Ann Arbor. 97 pages. 1953, Charles C Thomas, Springfield, Illinois. $3.25.

Physiological and Therapeutic Effects of Corticotropin (ACTH) and Cortisone. By Dwight J. Ingle, Ph.D., Senior Research Scientist, Research Laboratories, The Upjohn Company, Kalamazoo; and Burton L. Baker, Ph.D., Professor of Anatomy, University of Michigan Medical School, Ann Arbor, Michigan. 172 pages. 1953, Charles C Thomas, Springfield, Illinois. $5.50.

The Grassi Block Substitution Test for Measuring Organic Brain Pathology. By Joseph R. Grassi, A.B., M.A., Director of Clinical Psychology, Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, North Carolina. 74 pages. 1953, Charles C Thomas, Springfield, Illinois. $3.00.

The Neurophysiological Basis of Mind; The Principles of Neurophysiology. The Waynflete Lectures, delivered in the College of St. Mary Magdalen, Oxford, 1952. By John Carew Eccles, Professor of Physiology, The Australian National University, Canberra, Australia. 314 pages with 89 figures. 1953, Oxford University Press, New York. $6.50.

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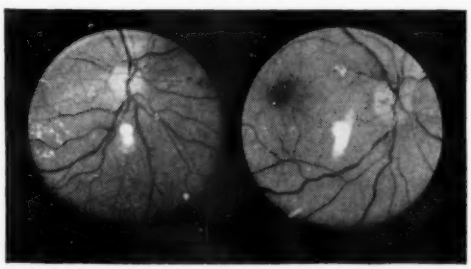

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1. Rogers, M. P., and Gray, C. L.: *Am. J. Digest. Dis.* 19:180, 1952.

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